Controlling Dangerous Pathogens
A Blueprint for U.S.-Russian Cooperation

A Report to the Cooperative Threat Reduction Program of
the U.S. Department of Defense

U.S.-Russian Collaborative Program for Research and Monitoring of Pathogens of
Global Importance Committee

National Academy of Sciences/Institute of Medicine/National Research Council

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ACRONYMS

ACDA	U.S. Arms Control and Disarmament Agency
AG	Australia Group
BW	biological weapons
BWC	Biological Weapons Convention
CBW	chemical and biological weapons
CDC	Centers for Disease Control and Prevention
CTR	Cooperative Threat Reduction
CW	chemical weapons
DOD	U.S. Department of Defense
DOE	U.S. Department of Energy
FDA	U.S. Food and Drug Administration
EMC	Division of Emerging and Other Communicable Diseases, Surveillance and Control
FSU	former Soviet Union
GCC	Gore-Chernomyrdin Commission
IOM	Institute of Medicine
IPP	U.S. Department of Energy Initiatives for Proliferation Prevention
ISTC	International Science and Technology Center
MOD	Russian Ministry of Defense
NAS	National Academy of Sciences
NIH	National Institutes of Health
OTA	Office of Technology Assessment
USAMRIID	U.S. Army Medical Research Institute of Infectious Diseases
USDA	U.S. Department of Agriculture
WHO	World Health Organization

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Preface

The National Academy of Sciences (NAS) created the Committee on International Security and Arms Control (CISAC) in 1980 to bring the scientific and technical resources of the Academy to bear on urgent problems of international peace and security. The primary initial activity of CISAC was a dialogue with Soviet counterparts that helped keep communication on nuclear arms control issues open during a time of great tension in U.S.-Soviet relations. In 1986, CISAC created a special working group on biological weapons control, which focused on another critical problem—developing improved methods of verification of the Biological Weapons Convention (BWC). The group carried out bilateral discussions with a counterpart group established under the aegis of the Soviet Academy of Sciences and then supported by the Russian Academy of Sciences.

Beginning in 1993 the working group became particularly concerned about potential proliferation of biological weapons (BW) know-how because of the economic difficulties that afflicted the former Soviet BW complex, along with other Russian institutions, after the collapse of the Soviet Union. At the same time, the group was impressed with the Russian expertise in the biological sciences and biotechnology. There appeared to be a good opportunity to draw on that experience in a cooperative effort to combat the global threat of emerging infectious diseases and promote U.S. national security interests. Members of the working group began to discuss this opportunity with appropriate officials of the U.S. government and encouraged efforts such as the decision of the International Science and Technology Center (ISTC) to fund appropriate research projects at former Soviet BW facilities. In 1995 the U.S. Department of Defense (DOD) asked CISAC for assistance in designing a program to expand bilateral cooperative efforts between U.S. scientists and their Russian counterparts who had been involved in the former Soviet BW program.

For assistance in developing the project, CISAC turned to two other parts of the Academy complex—the Board on International Health (BIH) of the Institute of Medicine (IOM) and the Office for Central Europe and Eurasia (OCEE) of the National Research Council. Both had extensive experience in areas directly relevant to fulfilling the DOD request. IOM has been concerned with the spread of infectious diseases; its 1992 report *Emerging Infections: Microbial Threats to Health in the United States* helped spark increased national and international attention to the risks posed by new and reemerging diseases.[1] For its part, OCEE had maintained contacts and exchanges with Soviet/Russian scientists for almost 40 years, acquiring unique experience and building an unmatched network of contacts. In October 1996, OCEE produced *An Assessment of the International Science and Technology Center (ISTC),* followed in 1997 by a related report, *Proliferation Concerns: Assessing U.S. Efforts to Help Contain Nuclear and Other Dangerous Materials and Technologies in the Former Soviet Union.*

NAS presented a proposal to DOD for developing a plan to increase U.S.-Russian research cooperation directed to the public health aspects of dangerous pathogens while furthering U.S. nonproliferation objectives. In addition to advancing the public health agendas of the two countries, NAS

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[1]In 1997, BIH released a white paper, *America's Vital Interest in Global Health,* which argued for collaborative U.S. engagement in activities similar to those discussed in this report.

believed that such cooperation also could build confidence at both the working and the government levels regarding compliance with international BW agreements.

The project began in the fall of 1996, with funding from the Cooperative Threat Reduction (CTR) Program, commonly referred to as the Nunn-Lugar Initiative. DOD provided CTR funds for supporting pilot research projects at Russian institutes to examine the potential for collaborative research activities that could be carried out effectively at facilities involved in the former Soviet BW program. A 14-member committee, which included members of the CISAC working group, the co-chair of BIH, and additional experts on BW and international health issues, developed the plan presented in this report with assistance from CISAC, BIH, and OCEE staff. Appendix A contains biographies of committee members and staff.

DOD charged the committee with emphasizing the conversion of former Soviet BW researchers to civilian work (see Appendix B for relevant excerpts from the contract). Since then, however, Congress has limited the mandate of the CTR program so that it no longer supports conversion activities as such. As a result, the committee focused on the related but broader nonproliferation goals that remain part of the CTR mandate. Early in its work and after discussions with DOD, the committee made two additional decisions. First, it decided to concentrate on Russia instead of the entire former Soviet Union. During the Soviet era there were limited BW facilities outside the Russian Federation; the major installation outside Russia, the Stepnogorsk standby production facility in Kazakhstan, is already the subject of a significant U.S. government redirection and dismantlement effort. Second, it focused its efforts on engaging the core of former Soviet BW personnel and facilities that had been involved in research on dangerous pathogens. The committee believes that U.S.-Russian cooperation in this domain—featuring direct laboratory-to-laboratory contacts and based on the principle of broad transparency—would benefit U.S. national security, public health, and economic interests as well as the advancement of fundamental science. The committee's rationale is presented in this report.

The committee believed that engaging Russian scientists and officials early in the planning effort was essential to the success of a long-term program of cooperation. To carry out this consultation and to gain firsthand knowledge of conditions and resources in former Soviet BW research facilities, a number of committee members and staff traveled to Russia on several occasions. Their visits are described in this report.

In developing the plan the committee was able to draw on the reports and studies of BW issues produced by many government agencies and nongovernment organizations, as well as individual policy and technical experts. Relevant U.S. government departments and organizations include the Department of State, Arms Control and Disarmament Agency, DOD, Department of Commerce, Central Intelligence Agency, and the Permanent Subcommittee on Investigations of the Governmental Affairs Committee of the U.S. Senate.

Among the academic institutions and nongovernment organizations and projects that have been interested in BW-related issues are the Chemical and Biological Arms Control Institute, the Harvard-Sussex Program on Chemical and Biological Weapons (CBW) Armament and Arms Limitation, the Henry L. Stimson Center, the New York Academy of Sciences, the Federation of American Scientists, the American Society of Microbiology, the Stockholm International Peace Research Institute, the Pugwash Conferences on Science and International Affairs, the Department of Peace Studies at the University of Bradford, Sandia National Laboratories, Lawrence Livermore National Laboratory, and the Monterey Institute for International Studies. Also, European scientists have been leading North Atlantic Treaty Organization workshops and projects on this topic. The *Declarations on Confidence-Building Measures* submitted each April since 1987 to the Centre for Disarmament Affairs at the United Nations by parties to the BWC provided particularly useful background information since they include U.S. and Russian declarations of past and present activities.

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Executive Summary

After extensive consultations with key Russian officials and scientific leaders and drawing on the experience gained through the initiation of six pilot projects at two Russian facilities to investigate the practical aspects of cooperation, the National Academy of Sciences Committee on U.S.-Russian Cooperation on Dangerous Pathogens recommends a five-year Pathogens Initiative, *followed by a second phase of sustained joint U.S.-Russian research and related efforts. The program will support collaboration on the epidemiology, prevention, diagnosis, and therapy of diseases associated with dangerous pathogens that pose serious public health threats, as well as related fundamental research. The* Pathogens Initiative *will engage a substantial number of highly qualified specialists from the former Soviet biological weapons complex and will serve important U.S. national security and public health goals.*

CONTEXT

Rapid advances in the biological sciences and biotechnology hold the promise of dramatically improving human health, agriculture, and other aspects of life. The broad diffusion of knowledge and capabilities enables many countries to benefit from these advances.

The spread of biotechnology, however, is also accompanied by significant risks. The capabilities associated with research on dangerous human, animal, and plant pathogens represent a complex dual-use technology; some of the knowledge of medicine, agriculture, and biotechnology overlaps with the knowledge necessary to use pathogens for hostile purposes. In addition, some equipment and facilities are versatile. Certain types of vaccine facilities, for example, could be converted to produce biological agents for use by military forces or terrorists.

The international community has responded to the threat of biological weapons (BW) by constructing an international regime—based on the Geneva Protocol and the Biological Weapons Convention (BWC) and supplemented by the Australia Group's export control guidelines—to ban their use, development, stockpiling, and production and to prevent countries and subnational groups from acquiring them. Activities focused on a particular country, such as Iraq, also are part of the international effort to forestall or respond to the proliferation of BW.

The BWC, however, lacks verification provisions and contains only limited procedures for addressing a suspected violation. Achieving a broad consensus on strengthening the international regime in this critical area is impeded by a number of factors, not least of which is a deep-seated lack of trust between Western countries and Russia concerning BW-related activities. In 1992, Russia acknowledged that the Soviet Union had maintained a BW program involving activities that violated the BWC, thereby confirming long-standing Western suspicions. At that time, President Yeltsin declared that illegal activities had ceased and future work in violation of the BWC was prohibited, but the Russian government has been unable to convince the United States that Russia is now in complete compliance with its treaty obligations.

Adding to these uncertainties is the sheer size of the former Soviet BW complex, which Russia is finding difficult to maintain financially, whatever the intended purpose of the facilities may now be.

Although in disrepair in many respects, this complex remains, raising fears in the West that dangerous materials, equipment, and know-how could be misused or could leak to parties of proliferation concern. Encouraging Russia to reconfigure some of these facilities to carry out peaceful work on dangerous pathogens and to convert the others to peaceful use not connected with dangerous pathogens is thus an important aspect of U.S. nonproliferation policy.

THE IMPORTANCE OF U.S.-RUSSIAN COOPERATION ON DANGEROUS PATHOGENS

Russia will undoubtedly continue to support legitimate research and related activities on dangerous pathogens. U.S. involvement in these activities through cooperative programs will provide opportunities to build confidence that prohibited research is not being pursued under the guise of legitimate undertakings. Also, from a public health viewpoint, Russian scientists who participated in former Soviet BW program have a unique knowledge of many aspects of naturally occurring pathogens as well as those that could be used by terrorist groups.

The committee believes that appropriately structured U.S.-Russian cooperation on dangerous pathogens—featuring direct laboratory-to-laboratory contacts and based on the principle of broad transparency—will serve the interests of both countries. Such cooperation could contribute significantly to the following objectives:

1. National security benefits
   - Providing greater mutual confidence about compliance with the BWC than would otherwise be possible
   - Reducing proliferation incentives
   - Serving as a stepping stone to dismantlement opportunities
   - Reconfiguring former Soviet BW-related activities
   - Enhancing capabilities to combat bioterrorism
2. Public health benefits
   - Improving understanding of the prevalence and characteristics of pathogens that pose threats to public health
   - Strengthening capabilities to prevent, diagnose, and treat outbreaks of infectious diseases
   - Enhancing international communications concerning disease trends and outbreaks
3. Economic benefits
   - Improving the stability of Russian research institutes by increasing the commercial viability of their research products
   - Leveraging limited national financial and human resources to serve national security public health
   - Providing new opportunities for the U.S. private sector to become more active in Russia
4. Scientific benefits
   - Enhancing the base of fundamental knowledge about pathogenesis
   - Increasing the international availability of research results.

Even the most extensive collaboration between Russian and U.S. scientists will not provide incontrovertible assurance that all research activities on dangerous pathogens are devoted to legitimate purposes. Recognizing this risk, the committee has concluded that, governed by appropriate rules of transparency, a cooperative program can be carried out in a manner to ensure that the risk of abuse of such a program is reduced to an acceptable level.

Expanded arrangements to provide sufficient transparency should include mutual agreement on a project-by-project basis concerning the activities that are legitimate; regular and agreed-upon access to

facilities, personnel, and information; and commitment to the principle that providing assurance is an active rather than a passive responsibility. Moreover, during the evaluation of any joint research project, its potential contributions to health and national security must be judged to outweigh the risk that the project might contribute to the development or improvement of offensive BW capabilities.

The committee recommends that the proposed program be undertaken in close coordination with related bilateral activities (see Table E-1).

Table E-1 Selected Organizations with Program Interests Related to the *Pathogens Initiative*

Organization	Description
International Science and Technology Center (ISTC)	This international organization, established by the United States, the European Union, Japan, and Russia, has supported a number of projects at a variety of institutes involved in the former Soviet BW program, including projects that address dangerous pathogens. ISTC has received dozens of other well-developed, but yet-to-be-funded proposals in this area. In addition, it has sponsored several symposia on related topics.
Initiatives for Proliferation Prevention (IPP)	This program of the U.S. Department of Energy recently announced its intention to support biotechnology proposals at Russian institutes, particularly Biopreparat institutes, that have potential for commercial markets. IPP has received dozens of proposals from a variety of Russian institutions, including proposals for research on dangerous pathogens.
U.S. Civilian Research and Development Foundation (CRDF)	This private foundation, established by Congress in 1992 and set up by the National Science Foundation in 1995, has solicited basic research proposals from interested Russian investigators in the biomedical field. CRDF currently supports eight projects at institutes that were part of the former Soviet BW complex. The future of additional competitions is subject to further funding.
National Aeronautics and Space Administration (NASA)	NASA has funded several projects at Biopreparat institutes in support of its space science activities. The future of these types of projects in Russia is uncertain.
Centers for Disease Control and Prevention (CDC)	The CDC has long-standing relationships with several Russian institutes, some of which participated in the former Soviet BW program. It has participated in activities in Russia supported by the U.S. Agency for International Development and frequently provides training for Russian scientists.
National Institutes of Health (NIH)	NIH provides grant supplements to its U.S. investigators to involve international scientists in their projects. NIH also provides training opportunities for international specialists in its laboratories. Russian researchers who participated in former Soviet BW activities can apply to these programs.
U.S. Department of Agriculture (USDA)	The USDA supports a limited number of biotechnology projects in Russia that are directly linked to agriculture development. Its current Russian portfolio does not include research on dangerous pathogens.

ESTABLISHING THE BASIS FOR EXPANDED COOPERATION

The committee's consultations with a range of Russian officials, research managers, and laboratory scientists helped ensure that assessments of the technical basis for cooperation were authoritative and realistic. In addition, these interactions resulted in Russian specialists, acquiring a sense of genuine partnership in the development of the recommended program. Consultations included scientific visits to Russian research institutes in Koltsovo and Obolensk, where pilot projects were later established; one round of consultations and two joint planning meetings in Moscow; and an international symposium in the Kirov region involving 30 Russian specialists, sponsored by the National Academy of Sciences (NAS) and the International Science and Technology Center (ISTC).

Of particular importance is the reported endorsement by the Russian Defense Council of the NAS initiative. Such support would be critical to the future success of a cooperative program involving defense scientists.

Biopreparat—an organization originally established by the Soviet government to provide a wide range of BW-related research, production, and support services—was the principal point of contact in Russia for the NAS committee. Specialists from many Biopreparat facilities and other Russian organizations participated in these consultations.

The committee was not successful in its efforts to meet with specialists from the Russian Ministry of Defense (MOD), but efforts to engage MOD should continue. Several Russian officials have expressed optimism that MOD will eventually participate in bilateral cooperative activities, either directly or in partnership with Biopreparat institutes. Although MOD participation is highly desirable, the Biopreparat complex provided much of the critical research and development support for the Soviet program; thus, the committee believes that cooperation with Biopreparat in and of itself will make a valuable contribution to achieving the benefits mentioned above.

In parallel with these consultations, the committee initiated six pilot projects at two Russian facilities and is developing two more (see Box E-1) to gain experience conducting collaborative research projects. The projects have contributed useful insights at the scientist-to-scientist level into the capabilities of the two countries. The pilot projects also were important in convincing Russian colleagues that the NAS undertaking was a serious endeavor with strong backing from the U.S. government, thereby encouraging them to participate actively in planning a long-term program.

Box E-1 Pilot Projects Initiated by NAS and Financed by DOD

The following projects were under way as of July 1997, with funds committed to Russian institutions[a]:

At the State Research Center for Virology and Biotechnology, "Vector," Koltsovo

- Study of prevalence, genotype distribution, and molecular variability of isolates of hepatitis C virus in the Asian part of Russia; $55,000; principal investigator, Sergei Netesov; collaborator, Elizabeth Robertson, CDC; ISTC 883
- Monkeypox virus genome; $55,000; principal investigator, Sergei Shchelkunov; collaborators, Peter Jahrling, USAMRIID, and Joseph Esposito, CDC; ISTC 884
- Study of the genetic and serologic diversity of hantaviruses in the Asian part of Russia; $55,000; principal investigator, Lyudmilla Yashina; collaborators, Connie Schmaljohn, USAMRIID, and Stuart Nichol, CDC; ISTC 805
- Development of advanced diagnostic kit for opisthorchiasis in human patients; $55,000; principal investigator, Valery Loktev; collaborator, Victor Tsang, CDC; ISTC 691

At the State Research Center for Applied Microbiology, Obolensk

- Molecular-biological and immunochemical analysis of clinical strains of tuberculosis and mycobacteriosis; $138,000; principal investigator, Igor Shemyakin; collaborator, Thomas Shinnick, CDC; ISTC 810
- Investigation of the immunological effectiveness of delivery *in vivo* of the *Brucella* main outer membrane protein by the anthrax toxin components; $61,500; principal investigator, Anatoly Noskov; collaborators, John Collier, Harvard University, and Arthur Friedlander, USAMRIID; ISTC 919

The following projects were being processed by ISTC as of October 1997:

At the State Research Center for Virology and Biotechnology, "Vector," Koltsovo

- Experimental studies of antiviral activities of glycyrrhyzic acid derivatives against Marburg, Ebola, and human immunodeficiency virus; principal investigator, Andrei Pokrovsky; collaborator, John Huggins, USAMRIID.

At the State Research Center for Applied Microbiology, Obolensk:

- Monitoring of Anthrax; principal investigator, Nikolai Staritsin; collaborator, Arthur Friedlander, USAMRIID.

NOTE: CDC = Centers for Disease Control and Prevention; DOD = Department of Defense; USAMRIID = U.S. Army Medical Research Institute of Infectious Diseases.

[a] Funds committed to U.S. collaborating institutions are CDC, $47,000; USAMRIID, $20,000; Harvard University, $9,000.

The NAS committee used the following criteria in selecting the pilot projects:

- Scientific importance of the topic;
- Quality of the proposal;
- Quality or capacity of the principal investigator, research team, and facilities;
- Provision for strong U.S. collaboration;
- Engagement of former Soviet BW expertise; and
- Promotion of transparency.

The committee also made the judgment that each project's potential contributions to public health or U.S. national security interests outweigh the risk that the project might contribute to the development or improvement of offensive BW capabilities.

The pilot projects were limited efforts, and the committee concluded that the following additional criteria should be considered in the selection of projects within the larger program recommended in this report:

- Likelihood of sustaining the research by attracting the interest of other organizations with financial capabilities to continue work in the general field after completion of the project and
- Promotion of linkages between Russian scientists working in institutions that had been involved in BW activities and those that were not involved in such activities.

The committee also strongly recommends that if future joint activities are pursued, U.S. specialists should adopt a more proactive role in identifying possible research topics and proposals for funding. The framework for collaboration presented in this report is designed to promote this goal.

The NAS became a partner of the ISTC in Moscow, which provides an important administrative framework for processing and reviewing proposals, monitoring projects, and dispensing funds within Russia. Of special importance are ISTC procedures for distributing funds for salaries directly to individual researchers, thereby circumventing opportunities for intermediaries to divert a portion of the funds for unintended uses.

Drawing on this first-hand experience, the committee developed three overarching principles for guiding bilateral activities:

1. Projects should be collaborative in design and conduct.
   - Only projects that are of interest to specialists in both countries should be undertaken.
   - All projects should be conducted on the basis of cooperation, not assistance, with each side making intellectual, financial, and in-kind contributions.
   - All relevant constituencies in both countries should be able to apply for participation in the program.
2. Projects should be designed and conducted in a way that maximizes transparency.
   - Activities should be carried out in an environment of openness.
   - Direct contacts among specialists should be stressed.
   - A central coordination point within each government should be apprised of cooperative activities.
3. Results of cooperative projects should be disseminated to the widest possible interested audience.
   - Whenever possible, research results should be promptly published or made available to international audiences through other channels.
   - Intellectual property and sensitive findings should be protected.
   - Intellectual property rights resulting from cooperative activities should be shared by the participating institutions on fair and equitable terms.

PHASE 1: A *PATHOGENS INITIATIVE*

Although Russian interest in cooperation in this field is increasing, the future political course in Russia remains difficult to predict. As cooperation becomes more ingrained in the Russian scientific community, joint efforts are more likely to survive political shocks, thus underscoring the importance of establishing and broadening cooperation while the window of opportunity is open.

The core of a *Pathogens Initiative* should be joint research projects directed to the epidemiology, prophylaxis, diagnosis, and therapy of diseases associated with dangerous pathogens as well as related fundamental research. According to Russian colleagues, if the U.S. government decides to support such an initiative, early intergovernment endorsement of the program could encourage MOD to participate. In addition, such political support could help resolve many policy, implementation, and budget issues confronting Biopreparat and other interested organizations in both countries.

The committee recommends seven program areas as the initial framework for the program. The first five areas—anthrax, melioidosis and glanders, plague, orthopox virus, and viral hemorrhagic fevers—are agents or diseases that have been linked with BW activities for many years. In each of these areas the Soviet government is believed to have invested substantial financial resources to carry out

research that is largely unknown outside that country. Organizations in the United States also have good research capabilities to help combat the infectious diseases of interest.

Two additional program areas will provide opportunities to address other pathogens or diseases of public health concern and to carry out related fundamental research. These two categories are particularly important in both providing support for key Russian scientists who are interested in pursuing careers not tied directly to potential BW agents and expanding the pool of potential collaborators in the United States.

A five-year program that builds to a level at which 15 three-year projects are initiated each year, involving an average of 10 full-time Russian specialists per project, could engage a substantial number of leading Russian specialists in the field and most of the key Russian research facilities. See Table E-2 for the phasing of collaborative research projects.

Table E-2 Phasing of Collaborative Research Projects

Task Name	1997 Y1	1998 Y2	1999 Y3	2000 Y4	2001 Y5	2002 Y6	2003 Y7	2004 Y8	2005 Y9	2006 Y10
Six pilot projects										
Two pilot projects										
Ten projects										
Twelve projects										
Fifteen projects										
Fifteen projects										
Fifteen projects										
Era of Sustained Cooperation										

Projects will be selected on a competitive basis by using the criteria set forth above. The resources devoted to each program area should depend on the quality of project proposals across all areas. The pilot projects fall into several areas, and the possibility of expanding these limited efforts should be considered if the results are promising.

Several supporting activities could effectively complement the research programs. Specifically, upgrading the communications capabilities of selected Russian institutes, improving the safekeeping and utilization of strain collections used as national reference standards, and expanding exchanges of information on biosafety requirements and practices are appropriate areas of cooperation.

In addition to annual reviews of all projects, the overall approach will be evaluated in depth at the end of the second year and adjusted as necessary.

PHASE 2: AN ERA OF SUSTAINED COOPERATION FOLLOWING THE *PATHOGENS INITIATIVE*

Recognizing that sustained cooperation must be accompanied by rules of disclosure and other measures designed to provide assurance that work is devoted strictly to legitimate purposes, the committee developed a model for progressive development of suitable transparency arrangements. The model is intended to emphasize the importance of transparency and to stimulate the official deliberations necessary to work out agreed-upon provisions. The model calls for an intergovernment mechanism to provide direction for collaborative efforts on a broad front.

Joint research projects would continue to be the core of long-term cooperation. Expanded cooperation in epidemiology and rapid response to outbreaks of infectious disease would promote trust between the two countries. Related to the expanded international exchange of data, the internal capabilities of Russia to assess and process epidemiologic information would have to be strengthened. During outbreaks of diseases, specialists from the two countries should collaborate in providing their

most relevant information and offering technical support to each other. Also, Russian specialists who are involved in field investigations should be encouraged to apply for participation in the training programs of the Centers for Disease Control and Prevention (CDC).

In addition, the promotion of effective national regulatory approaches to controlling dangerous pathogens appears to be essential to ensure responsible handling of these pathogens on a broad front. Effective enforcement procedures and sharing of experiences are particularly important in developing mutual trust.

At the same time, the need to prevent the dissemination of sensitive information to parties of proliferation concern and to protect intellectual property rights would continue to be important. The Russian and U.S. governments should adopt appropriate procedures to ensure that these issues are addressed in a manner that does not undercut the broader transparency objectives of cooperative endeavors.

COSTS

To build on current momentum, the committee recommends that the U.S. Department of Defense (DOD) promptly provide financial support for the *Pathogens Initiative*. Sustained funding for the longer-term Phase 2 program would undoubtedly require agreement between the executive branch and Congress about a line item in the budget of a selected agency. It is premature to speculate which department or agency should have long-term financial responsibility.

Pathogens Initiative

The projected costs to the United States of the *Pathogens Initiative* are as follows: fiscal year (FY) 1998, $6 million; FY 1999, $7 million; FY 2000, $8.5 million; FY 2001, $8.5 million; and FY 2002, $8.5 million. Most of these funds are earmarked for direct project support, as shown in Table E-3. When the *Pathogens Initiative* is fully developed in FY 2000, the costs will be $4.5 million (53 percent) for the Russian research teams, $2.5 million (29 percent) for the U.S. collaborators, $500,000 (6 percent) for project development activities, and $1 million (12 percent) for program evaluation, financial management, and related support activities.

Table E-3 Allocation of Funds per Fiscal Year During the *Pathogens Initiative* (in millions of dollars)

FY	Budget	New Projects	Total Projects[a]	Funds to Russian Research Teams	Funds to U.S. Collaborator	Funds to Project Management
1998	6.0	10	10	3.5	1.5	1.0
1999	7.0	12	22	4.0	2.0	1.0
2000	8.5	15	37	4.5	2.5	1.5
2001	8.5	15	42	4.5	2.5	1.5
2002	8.5	15	45	4.5	2.5	1.5

[a] This total does not include pilot projects.

Phase 2: An Era of Longer-Term Sustained Cooperation

As indicated above, it is assumed that the size of the program will grow steadily and then level off during the era of sustained cooperation. Under the model suggested as a goal for expanded efforts, the estimated annual costs to the United States beginning in FY 2003 are $5 million (50 percent) to support U.S. collaborators; $2 million (20 percent) to support selected aspects of Russian participation in activities of special interest to the United States; $1 million (10 percent) for project development,

evaluation, and related activities; and $2 million (20 percent) for support for the intergovernment mechanism and related specialized committees to oversee the entire activity. The total U.S. contribution would be $10 million per year and Russian institutions would be expected to cover most of their own costs.

ANTICIPATED RESULTS OF THE PROGRAM

The proposed joint efforts could build a considerable level of trust between the scientific communities of Russia and the United States in a way that would help change the tone of diplomacy on the international security aspects of dangerous pathogens. Such efforts could have profound effects–both direct and indirect–in reducing the threats of proliferation and terrorism. Also, the program will make many contributions to combating dangerous infectious diseases, while serving as a model for global efforts when the dangers of new and reemerging diseases are being recognized more fully in many countries.

One likely effect of such a multiyear program in Russia is a structural adjustment of its research enterprise dealing with dangerous pathogens. Research projects will be increasingly concentrated at a handful of the best institutions, which would become centers of excellence. To the extent that other institutions remain viable, they should be motivated to find work outside the area of dangerous pathogens.

Thus, there is a high probability this program will help achieve DOD objectives of nonproliferation and reconfiguration of the former Soviet BW complex into a less diffuse, less uncertain, and more public health oriented establishment.

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The Context for a Program of Bilateral Cooperation

THE DUAL-USE DIMENSION OF BIOTECHNOLOGY

As we approach the turn of the century, rapid advances in the biological sciences and biotechnology hold the promise of dramatically improving human health, agriculture, and other aspects of life. Although most discoveries and innovations have originated in the advanced industrial countries, broad diffusion of knowledge and capabilities provides the opportunity for other countries to use the results of these advances as well.

The spread of biotechnology, however, is accompanied by potential risks. The capabilities associated with research on dangerous human, animal, and plant pathogens represent a complex dual-use technology; some of the knowledge of medicine, agriculture, and biotechnology overlaps with the knowledge necessary to use pathogens for hostile purposes.[1] In addition, certain equipment and facilities are versatile; some vaccine facilities, for example, could be converted to produce biological agents for use by military forces or terrorists.[2]

Although under some conditions, biological weapons (BW) could in principle produce the same casualty levels as nuclear weapons of comparable weight, the feasibility of achieving these and other effects is far less certain. This uncertainty has led many experts to conclude that BW are generally unattractive, at least for traditional tactical military purposes.[3] However, the determined efforts of Iraq to develop a BW capability suggest that some countries may not share this assessment. An estimate by the Office of Technology Assessment (OTA) in 1993 named eight countries "generally reported as having an undeclared offensive biological warfare program."[4] In 1996, U.S. Arms Control and Disarmament Agency Director (ACDA) John Holum cited a dozen unspecified countries, noting that the United States believed this was twice as many countries as when the Biological Weapons Convention (BWC) entered into force in 1975.[5] In 1997 the U.S. Department of Defense Quadrennial Defense Review concluded that

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[1] For the purposes of this report, dangerous pathogens are defined as pathogens that are highly infectious, causing great concern to global public health. Of particular interest are pathogens that could be used in biological warfare.

[2] The *Journal of the American Medical Association* (JAMA) devoted an entire issue (vol. 278, no. 5, August 6, 1997) to the subject of biological warfare and bioterrorism.

[3] Office of Technology Assessment, U.S. Congress. 1993. *Proliferation of Weapons of Mass Destruction: Assessing the Risks*. Washington, D.C.: U.S. Government Printing Office, pp. 52-62; International Institute for Strategic Studies, 1997. *Strategic Survey 1996/1997*. London, p. 37.

[4] OTA, op. cit., p. 65. The countries were Iran, Iraq, Israel, Libya, Syria, China, North Korea, and Taiwan. To appear on the OTA list, a country must have been named in at least four of six major unclassified studies (five American and one Russian).

[5] U.S. ACDA, Washington, D.C. 1996. The Honorable John D. Holum, Director, Remarks to the Fourth Review Conference of the Biological Weapons Convention, Geneva, Switzerland, November 26.

"the threat or use of chemical and biological weapons (CBW) is a likely condition of future warfare, including in the early stages of war to disrupt U.S. operations and logistics."[6]

In addition to the risk of countries developing BW as an agent of war, there is growing concern that terrorists might add BW to their arsenals.[7] Terrorist use of biological agents could cause extensive casualties—and terrorists may not be as concerned about precision, predictability, and timeliness as regular military forces. Furthermore, a massive infrastructure is not necessary to create a deadly arsenal of these weapons.[8] To date, terrorist use has been confined to a few small incidents affecting a limited number of people. However, the efforts of the Aum Shinrikyo cult to master biological agents for broader use, although never fully realized, underscore the potential threat.[9]

Preventing, deterring, and responding to the risks posed by the availability of BW thus constitute a key security challenge facing the United States and the international community in the post-Cold War period.

INTERNATIONAL RESPONSE TO THE BW THREAT

The international community has responded to the threat of BW by constructing an international regime to ban their development, production, stockpiling, and use and to prevent countries and subnational groups from acquiring them. The 1925 Geneva Protocol prohibits the use of "bacteriological methods of warfare" as well as chemical weapons in war (see Appendix D for full text). Since the protocol bans only the *use* of bacteriological (biological) methods of warfare, a number of countries, including the United States and the former Soviet Union, developed offensive and defensive BW capabilities.[10] In 1969, however, President Nixon unconditionally renounced U.S. involvement in all methods of biological warfare, paving the way for negotiation of the 1972 BWC. (See Appendix E for full text.)

The BWC goes beyond the Geneva Protocol to ban the development, production, and stockpiling of bacteriological (biological) weapons and their means of delivery. Article X of the BWC explicitly permits research on and use of biological agents and toxins for peaceful purposes, acknowledging the fundamental dual-use dilemma. (The Treaty on the Nonproliferation of Nuclear Weapons and the Chemical Weapons Convention also contain provisions recognizing that nonproliferation measures should not deny parties to the treaty access to the peaceful benefits of technology.) Article X further declares that states parties "in a position to do so shall also cooperate in contributing individually or together with other states or international organizations to the further development and application of

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[6] U.S. Department of Defense (DOD). 1997. *Report of the Quadrennial Defense Review*. Washington, D.C.: DOD Office of Public Affairs, p. 13.

[7] See, for example, Kaufmann, A. F., Meltzer, M. L., and Schmid, G. P. 1997. The economic impact of a bioterrorist attack: Are prevention and postattack intervention programs justified? *Emerg. Infect. Dis.* 3: 83-94.

[8] Director of Central Intelligence. 1997. The Acquisition of Technology Relating to Weapons of Mass Destruction and Advanced Conventional Munitions, July-December 1996. Washington, D.C.: U.S. Government Printing Office, p. 3.

[9] Olson, K. B. 1995. Testimony to the Permanent Subcommittee on Investigations of the Senate Committee on Government Affairs, October 31, p.16. The Aum cult was unsuccessful in its attempts to develop and use effective biological agents; whether the group would have succeeded eventually cannot be known. See Kaplan, D. E. and Marshall, A. 1996. *The Cult at the End of the World*. New York, N.Y.: Crown Publishers.

[10] In addition, a number of countries, including the United States, did not promptly ratify the protocol. U.S. ratification of the protocol came in 1975 at the same time as its ratification of the BWC. The Soviet Union ratified the Geneva Protocol in 1928 and the BWC in 1975. See ACDA. 1990. *Arms Control and Disarmament Agreements: Texts and Histories of the Negotiations*. Washington, D.C.: U.S. Government Printing Office, pp. 15-18.

scientific discoveries in the field of bacteriology (biology) for prevention of diseases, or for other peaceful purposes."[11]

The BWC, however, lacks verification provisions and contains only limited procedures for addressing a suspected violation.[12] Conferences have been held every five years since 1981 to review the treaty's status and progress. In 1986 the Second Review Conference adopted a number of confidence-building measures, including exchanges of information about national capabilities and activities in BWC-relevant areas. In 1991 the Third Review Conference added more measures. See Box 1-1 for a list of the measures adopted in 1986 and 1991. The Third Review Conference also created an international group of technical experts to examine the scientific and technical possibilities for BWC verification.[13] As of mid-1997, an ad hoc group, in which all states parties to the treaty could participate, had begun negotiation of a legally binding verification protocol. Achieving a broad consensus on strengthening the international regime in this critical area is impeded by a number of factors, not least of which is a deep-seated lack of trust between the Western countries and Russia about BW-related activities. (The principal issues related to Russia are discussed in the next section.)

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[11] Ibid., pp. 133-138.

[12] In the event of a suspected violation, a state party to the convention can call for consultation among the states parties and suggest an appeal to the United Nations Security Council.

[13] Dando, M. R., and Pearson, G. S. 1997. The Fourth Review Conference of the Biological and Toxin Weapons Convention: Issues, outcomes, and unfinished business. *Politics Life Sci.* 16: 118-120.

BOX 1-1 Confidence-Building Measures Adopted by the Second and Third BWC Review Conferences (1986 and 1991)

A. Exchange of data on research centers and laboratories: Exchange of data, including name, location, scope, and general description of activities, on research centers and laboratories that meet very high national or international safety standards established for handling, for permitted purposes, biological materials that pose a high individual and community risk or specialize in permitted biological activities directly related to the Convention (1986).

B. Exchange of information on outbreaks of infectious diseases and similar occurrences caused by toxins: Exchange of information on outbreaks of infectious diseases and similar occurrences caused by toxins and on all such events that seem to deviate from the normal pattern as regards type, development, place, or time of occurrence. The information provided on events that deviate from the norm will include, as soon as it is available, data on the type of disease, approximate area affected, and number of cases (1986).

C. Encouragement of publication of results and promotion of use of knowledge: Encouragement of publication of results of biological research directly related to the Convention, in scientific journals generally available to States Parties, as well as promotion of use for permitted purposes of knowledge gained in this research (1986).

D. Active promotion of contacts: Active promotion of contacts between scientists, other experts and facilities engaged in biological research directly related to the Convention, including exchanges and visits for joint research on a mutually agreed basis (1986).

Modalities: In order to actively promote professional contacts between scientists, joint research projects and other activities aimed at preventing or reducing the occurrence of ambiguities, doubts, and suspicions and at improving international cooperation in the field of peaceful bacteriological (biological) activities, States Parties are encouraged to provide information, to the extent possible, on planned international conferences, seminars, symposia, and similar events dealing with biological research directly related to the Convention and on other opportunities for exchange of scientists, joint research, or other measures to promote contacts between scientists engaged in biological research directly related to the Convention (1991).

E. As an indication of the measures which they have taken to implement the Convention, States Parties shall declare whether they have legislation, regulation or other measures: a) to prohibit the development, production, stockpiling, acquisition or retention of microbial or other biological agents, or toxins, weapons, equipment and means of delivery, specified in Article I of the Convention, within their territory or anywhere under their jurisdiction or control; b) in relation to the export or import of micro-organisms pathogenic to man, animals and plants or of toxins in accordance with the Convention; States Parties shall complete the attached Form E and shall be prepared to submit copies of the legislation, or regulations or written details of other measures on request to the UN Department of Disarmament Affairs or to an individual State Party. On an annual basis States Parties shall indicate, also on the attached form, whether or not there has been any amendment to their legislation, regulations or other measures (1991).

F. In the interest of increasing transparency and openness, States Parties shall declare whether or not they conducted any offensive and/or defensive biological research and development programs since 1 January 1946. If so, States Parties shall provide information on such programs, in accordance with Form F (1991).

G. To further increase the transparency of biological research and development related to the Convention and to broaden scientific and technical knowledge as agreed in Article X, each State Party will declare all facilities, both governmental and non-governmental, within its territory or under its jurisdiction or control anywhere, producing vaccines licensed by the State Party for the protection of humans. Information shall be provided on Form G attached (1991).

Complementing Article III of the BWC, which prohibits transfer of items or assistance to any state, group of states, or international organizations in contravention of the BWC, many states have enacted national export control regulations. In an attempt to harmonize these regulations, some 30 states have entered into an informal coordination mechanism known as the Australia Group, which has developed lists of microorganisms and toxins, as well as equipment, that could be used for BW. These

lists are intended to help guide the national export control decisions of its members. (See Appendix F for the lists.)[14]

Activities focused on particular countries are another part of the international effort to forestall or respond to the proliferation of BW. At present, the primary case of country-specific action is Iraq, which remains subject to stringent UN-imposed sanctions and continuing inspections in the wake of revelations after the Persian Gulf War of its attempts to develop nuclear and biological weapons.[15] The United States also has made certain other countries a particular focus of its counterproliferation initiatives and has sought the cooperation of its allies to limit the access of these countries to weapons of mass destruction and their means of delivery.[16]

THE SPECIAL CASE OF RUSSIA

Russia is of special concern to the United States as a source of proliferation. When the Soviet Union collapsed in 1991, Russia inherited most of the vast Soviet military establishment. What remains exceeds anything that Russia can afford to maintain; this excess capacity has heightened concerns about the proliferation of dangerous materials, equipment, technical data, and know-how.

In the immediate aftermath of the Soviet collapse, U.S. concern focused on the safety and security of Soviet nuclear weapons. In response, Congress passed the Soviet Nuclear Threat Reduction Act (often referred to as the Nunn-Lugar Initiative) in late 1991 to provide a basis for U.S. cooperation with the former Soviet Union (FSU). Its primary purposes were to prevent proliferation of dangerous or potentially dangerous items and technology from the nuclear weapons complex of the FSU and to facilitate implementation of arms reduction agreements. The ensuing Cooperative Threat Reduction (CTR) program, administered by the Department of Defense (DOD), was designed to limit the proliferation potential of both weapons and technical experts. Thus, in addition to programs to secure weapons and material, the CTR program provided initial funding for the International Science and Technology Center (ISTC) as a means of redirecting former weapons scientists and engineers to new, peaceful research endeavors and promoting U.S. nonproliferation interests.[17]

The former Soviet BW program was also causing concern in the international community. In 1992, Russia acknowledged that the Soviet Union had maintained a BW program involving activities that violated the BWC, thereby confirming long-standing Western suspicions.[18] At its peak, the research and development component of the Soviet program supported basic research in both military and nonmilitary institutions to ensure the availability of fundamental knowledge and expertise; maintained a network of specialized research facilities, the Biopreparat complex, which was responsible for weapons-related research and production of agents as well as development and production of vaccines and other defensive

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[14] The Australia Group (AG) was originally created to foster consistent export controls related to chemical weapons; in 1990 the AG expanded its scope to include BW issues.

[15] Iraq had already developed and used chemical weapons (CW) both during its war with Iran in the late 1980s and on its own citizens. After the Gulf War, the Iraqi CW program was included in UN sanctions.

[16] See, for example, Perry, W. J., Secretary of Defense. 1996. *Annual Report to the President and Congress*. Washington, D.C.: U.S. Government Printing Office, pp. 53-59.

[17] National Research Council. 1996. *An Assessment of the International Science and Technology Center.* Washington, D.C.: National Academy Press.

[18] Hunger, I. 1996. *Strengthening the BWC: Key Points for the Fourth Review Conference*, Pearson, G. S. and Dando, M. R., eds. Geneva: Quaker United Nations Office, p. 84. See also text of an interview with General Anatoly Kuntsevich in *Rossiskiye Vesti,* September 22, 1992, and FBIS-SOV-92-186, September 24, 1992. See also text of an interview with President Boris Yeltsin in *Rossiskiye Vesti,* May 27, 1992, and FBIS-SOV-92-103, May 27, 1992.

measures; and maintained highly secret research and production facilities within the Ministry of Defense (MOD), about which relatively little is known.[19] Boxes 1-2 thru 1-4 list selected MOD, Biopreparat, and civilian institutions.

BOX 1-2 MOD Institutes with Biological Research Programs

1. Scientific Research Institute of Microbiology, Kirov[a]
   - Center for Virology, Sergiev Posad[a]
   - Center of Military-Technical Problems of Biological Defense, Yekaterinburg
2. Scientific Research Institute of Military Medicine, St. Petersburg

NOTE: For discussions of the activities of these institutes, see Rimmington, A. 1996. From military to industrial complex? The conversion of biological weapons' facilities in the Russian Federation. *Contemp. Security Policy* 17: 80-112.

[a] Participated in ISTC Symposium in Pokrov in 1996.

Source: Committee Discussions in Russia, 1997.

Box 1-3 Selected Biopreparat Institutes and Enterprises with Capabilities of Relevance to Dangerous Pathogens That Have Expressed Interest in International Cooperation

1. Research Institutes
   - State Research Center for Virology and Biotechnology, "Vector," Koltsovo[a,b,c,d]
   - State Research Center for Applied Microbiology, Obolensk[a,b,c,d]
   - Institute of Immunology, Lyubuchany[b,c,d]
   - Institute for Scientific Biological Instrumentation, Moscow[b,c,d]
   - Institute for Highly Pure Biopreparations, St. Petersburg[d]
   - Institute for Biochemical Engineering, Moscow[d]
   - Research and Design Institute for the Biotechnology Industry, "Biotin," Kirov[c,e]
2. Scientific or production complexes
   - Scientific Experimental and Industrial Base, Omutninsk[c,d,e]
   - Biologics Plant, Pokrov[c]
   - Scientific Design Institute and Factory of Biopreparations Complex, Berdsk[e]

NOTE: Sources of information on the declared interests of most of these institutions are ISTC reports of the Kirov and Pokrov symposia and the unrestricted summaries of proposals submitted to the ISTC. Biopreparat officials informed the committee in June 1997 that there are 47 facilities within its complex, including 11 research institutes. Many facilities not listed above are undoubtedly interested in international cooperation, but their capabilities related to dangerous pathogens are unknown to the committee.

[a] Participated in pilot projects initiated by the National Academy of Sciences (NAS).

[b] Member of Biopreparat working group on bilateral cooperation.

[c] Participant or exhibitor at international symposium in Pokrov (1996) or Kirov (1997).

[d] Proposals sent to ISTC.

[e] Indication of interest conveyed informally to NAS.

[19] Rimmington, A. 1996. From military to industrial complex? The conversion of biological weapons facilities in the Russian Federation. *Contemp. Security Policy* 17: 80. It should be noted that there is little unclassified information available from the U.S. government about the size and activities of the Soviet BW research and production complex.

Box 1-4 Selected Russian Civilian Institutions Having Experience with Dangerous Pathogens and Links with Former BW-Related Specialists That Have Expressed Interest in International Cooperation

1. Ministry of Health, including Russian Academy of Medical Sciences
- Central Epidemiology Research Institute, Moscow[a,b]
- Ivanovsky Institute of Virology, Moscow[a,b,c,d]
- Gamaleya Institute of Epidemiology and Microbiology, Moscow[b,d]
- Chumakov Institute of Poliomyelitis and Viral Encephalitides, Moscow[d]
- Tarasevich Research Institute of Standards and Control, Moscow[a,b]
- Institute of Immunology, Moscow
- Sechenov Academy of Medicine, Moscow[d]
- Scientific Research Institute for Vaccines and Sera, St.Petersburg[b]
- Research Center of Toxicology and Sanitary Regulation, Serpukhov[b]
- Plague Research Institute, Saratov[d,e]
- Plague Research Institute, Stavropol[d,e]

2. Russian Academy of Sciences
- Institute of Bioorganic Chemistry, Moscow[c]
- Institute of Gene Biology, Moscow[b]
- Institute of General Genetics, Moscow[b]

3. Ministry of Agriculture, including Academy of Agricultural Sciences
- All Russian Research Institute for Animal Protection, Vladimir[a]
- All Union Research Institute of Veterinary Preparations[a]

4. Other
- Volgo-Vyatka Applied Biotechnology Center, Kirov[a,e]
- Biysk Oleum Factory, Altai Region[b]
- Science and Technology Center Lekbiotech[b]
- Biotechnology Innovation Center, Serpukhov[b]

NOTE: This listing is not intended to be exhaustive, but it does cover most of the capabilities relevant to the *Pathogens Initiative.*

[a] Participant or exhibitor at international symposium in Pokrov (1996) or Kirov (1997).

[b] Proposals to ISTC.

[c] Leading role in previous projects with the National Academy of Sciences (NAS) related to dangerous pathogens.

[d] Member of Biopreparat working group on bilateral cooperation or participant in discussion in Petrovo-Dalnyee (1997).

[e] Interest in cooperation conveyed informally to NAS.

In 1992, Russian President Yeltsin issued a decree declaring that illegal activities had ceased and all future work in violation of the BWC was prohibited.[20] Despite this declaration, the Russian government has been unable to convince the United States that Russia is now in complete compliance with its treaty obligations.

In September 1992 the United States, the United Kingdom, and Russia signed a joint statement to create a mechanism for resolving lingering concerns and demonstrating the defensive nature of remaining Russian military capabilities in the BW area.[21] After initial reciprocal visits to selected facilities in each of the three countries, the governments were unable to agree on satisfactory arrangements for more extensive mutual visits or inspections. The Russian government has argued that the process also should serve to verify the legitimacy of U.S. and U.K. programs. Citing the lack of evidence of U.S. or U.K. noncompliance, the two governments reject this argument, maintaining that resolving the issue of

[20] Embassy of the Russian Federation, Washington, D.C. 1992. Decree of the President of the Russian Federation of 11 April 1992 (No. 390); and Rimmington, op. cit., p. 80.

[21] U.S. Department of State, Office of the Assistant Secretary/Spokesman. 1992. Joint U.S./U.K./Russian Statement on Biological Weapons. September 14.

Russian compliance is the only U.S. objective in pursuing the trilateral process. The trilateral process remains at an impasse, mired in mutual suspicion and recrimination.[22] ACDA Director Holum thus reported to the Fourth Review Conference of the BWC in December 1996 that "the challenge to demonstrate full eradication of that [Soviet] program still remains."[23]

Adding to these uncertainties is the sheer size of the former Soviet BW complex. For example, it is estimated that by the late 1970s, Biopreparat encompassed 50 research and development and production facilities and employed 100,000 people.[24] Russia is finding it difficult to maintain Biopreparat and other facilities financially, whatever their intended purpose may now be. Many elements of the complex still exist in some form, raising fears in the West that dangerous materials, equipment, and know-how could be misused or could leak to parties of proliferation concern. Encouraging Russia to reconfigure some facilities to carry out peaceful work on dangerous pathogens and to convert others to peaceful use not connected with dangerous pathogens is thus an important aspect of U.S. nonproliferation policy.

The CTR program and the ISTC expanded their efforts to include former BW facilities and specialists in 1994. During 1996 and 1997, a number of other U.S. government agencies began to show interest in cooperative programs with components of the former Soviet BW complex. (These programs are identified in Table E-1.) Like the ISTC projects, most of these activities support the redirection of former BW researchers and facilities to work on civilian problems not directly related to dangerous pathogens.

THE IMPORTANCE OF U.S.-RUSSIAN COOPERATION ON DANGEROUS PATHOGENS

The committee recognizes that Russia will continue to support legitimate research on dangerous pathogens, with a substantial portion probably concentrated in facilities of the former Soviet BW complex. The committee believes that it is in the best interests of the United States for American specialists to be actively engaged in collaborative research at these facilities. Such collaboration is important for two key reasons: (1) to provide a mechanism for increasing mutual assurance that activities related to dangerous pathogens are devoted to legitimate purposes and (2) to draw on the extensive Russian expertise in advancing the national and international knowledge base and public health capabilities related to prevention and control of dangerous infectious diseases.[25]

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[22] Dando and Pearson, op. cit., p. 108.

[23] U.S. ACDA, Washington, D.C. 1996. The Honorable John D. Holum, Director, Remarks to the Fourth Review Conference of the Biological Weapons Convention, Geneva, Switzerland, November 26. The head of the Russian delegation, Grigory Berdennikov, told the conference that the Russian Federation "adheres to all clauses of the convention and has never developed, produced, accumulated, or stored biological weapons" (Parrish, S. 1996. *Russia denies it has biological weapons.* OMRI Daily Digest, November 27). See also U.S. Arms Control and Disarmament Agency. 1996. *Threat Control Through Arms Control: Annual Report to Congress.* Washington, D.C.: U.S. ACDA, pp. 86-87.

[24] Rimmington, op. cit., p. 87. The estimate is based on translated Russian press reports and the authors' interviews with Biopreparat officials. Biopreparat officials told the committee that it currently has 40,000 employees, of whom approximately 1,000 are highly qualified scientists with specialized knowledge and skills relevant to dangerous pathogens.

[25] There is no evidence to support suspicions about U.S. noncompliance with the BWC. Based on the committee's experience in Russia, a number of Russians who will be key to successful implementation of the proposed *Pathogens Initiative*, nevertheless, harbor genuine suspicions about U.S. compliance with the BWC. The committee believes that it will thus be necessary to build the trust and confidence of the Russians over time; hence this report emphasizes the need for *mutual* assurance.

The five-year *Pathogens Initiative* and the subsequent Phase 2 model for sustained collaboration recommended in this report provide a framework for a more concerted effort for engaging the intellectual core of the former Soviet BW program. Although such collaboration should be effective in and of itself, the committee also believes that the proposed program must be linked to other U.S. government efforts to engage former Soviet BW scientists in collaborative research and public health activities extending beyond dangerous pathogens. In combination, these programs will promote the continued transition of former Soviet BW scientists into many areas of civilian research. In addition, by increasing linkages between the civilian and military sectors, transparency will increase, thereby further reducing the risk that collaborative research programs could contribute to illegal activities while enhancing the effects of scientific efforts.

In the committee's assessment, the benefits of carefully designed U.S.-Russian collaboration on research on dangerous pathogens—the focus of the *Pathogens Initiative*—far outweigh the risks, but the risks cannot and should not be ignored.

Transparency as a Response to Risk

The committee recognizes that even the most extensive collaboration between Russian and U.S. scientists will not provide incontrovertible assurance that all research activities on dangerous pathogens are in compliance with the BWC. No means has been identified to achieve such a standard. The committee is confident that there is little risk of abuse in the pilot projects in view of the transparency arrangements that include reciprocal on-site exchanges of project investigators. The committee has concluded that under the transparency arrangements described below, expanded cooperative activities can be carried out in a manner that ensures the risk of abuse of such a program is reduced to an acceptable level.

The expanded arrangements to enhance transparency envisioned for the *Pathogens Initiative* and its subsequent phase should include mutual agreement, on a project-by-project basis, as to activities that are legitimate; regular and agreed-upon access to facilities, personnel, and information; and a commitment to the principle that providing assurance is an active rather than a passive responsibility—for example, through regular reporting and consultation. Given inevitable dual-use concerns about research on dangerous pathogens, the committee believes that scientific collaboration with experts and facilities involved in BW programs must include all of these aspects of transparency. Moreover, for any collaborative project to be supported, its potential contributions to public health and U.S. national security objectives must be judged to outweigh the residual risk of abuse.

This level of transparency would be considerably beyond current practice. For example, the rules of access to facilities provided under the ISTC—20 days after proper notification—are not adequate for the kinds of dual-use technology represented by BW. These rules were negotiated in the context of international cooperation on nuclear issues—namely, access to the closed atomic cities of Russia—and were focused primarily on ISTC's financial oversight responsibilities (see Box 1-5). The committee believes, however, that these rules are very useful and represent the best that can be achieved within the ISTC context at present.

Box 1-5 ISTC Access Requirements for Individual Projects

- Identification in research proposal of all participants in a proposed project who have participated in biological defense activities, as well as identification of other participants
- Reports on project implementation, including quarterly technical progress reports, annual technical reports, and a final comprehensive report together with related financial reports
- With 20 days advance notice, access by financing party and its designees to all project activities and to complete information on facilities, equipment, documentation, information, data systems, materials, supplies, personnel, and services that are involved in the project
- Right of Russian institution to protect those portions of facilities not involved in the project
- Records and documentation maintained for possible audit for two years after completion of project and availability of personnel for interviews about the project during this period

Source: ISTC Statute, Article XVI, March 17, 1994, and ISTC procedures as of July 1997.

If adopted, the *Pathogens Initiative* will offer additional layers of protection against potential abuse of the projects by building stronger, more direct, and sustained ties between laboratories and researchers. By providing funds to permit U.S. researchers to visit and spend time in the laboratories of their Russian research collaborators, the *Pathogens Initiative* will provide broader and more frequent access—and hence confidence—than current ISTC arrangements can achieve.

1. Repeated visits to the same facilities in connection with a variety of projects will expand knowledge and insights beyond those that can be provided by the narrow ISTC requirements for individual visits.

2. As the *Pathogens Initiative* expands, it can be expected to provide access to new facilities and laboratories.

3. Sustained personal interactions among U.S. and Russian scientists involved in the joint research will provide insights beyond those required by ISTC.

4. Detailed understanding of problems encountered during the conduct of collaborative research will also provide new insights into Russian capabilities and programs.

The outcome of current negotiations to strengthen the BWC with a legally binding verification protocol could also influence the potential effectiveness of bilateral transparency arrangements. The current BWC confidence-building measures represent voluntary commitments that only a few countries regularly fulfill (see Box 1-1).[26] If the *Pathogens Initiative* is implemented in the context of a new protocol, risks will be further alleviated because this cooperative effort will be supported and complemented by the new verification arrangements. A situation without a protocol will be more difficult. In this instance the committee believes that it will be even more important to have the *Pathogens Initiative* as a key element of a coordinated U.S. government effort to fill the void.

Benefits

The benefits of U.S.-Russian collaboration on dangerous pathogens fall into four broad categories.

1. National security benefits

- Providing greater mutual confidence about compliance with the BWC than would otherwise be possible: As noted above, properly designed collaborative research projects can provide an important means for enhancing transparency: joint research, person-to-person contacts, regular exchanges of personnel, and direct access to facilities all promote transparency. Many defense scientists working in

[26] These countries include the United States, Russia, and the United Kingdom.

closed facilities have had little contact with civilian counterparts working on related problems.[27] Involving these scientists in research on public health problems could build bridges between military and civilian institutions and their personnel. Integrating them into international, as well as national, networks of researchers committed to the prevention and control of dangerous diseases should reinforce standards of ethics and social responsibility that counter the temptations of illegal activities. Providing opportunities for them to talk shop with colleagues and, as a result, to practice their trade and be valued for this contribution are strong incentives for complying with international norms.

- Reducing proliferation incentives: For several years, Russian scientists who possess extensive experience in handling pathogens with BW potential have left their institutes for new careers that promise better financial or scientific futures in Europe, the United States, and Israel.[28] Some of the remaining scientists may be tempting targets for states or terrorist groups in search of recruits or information on BW. Collaborative programs, with guaranteed paychecks and challenging research activities, can reduce the economic incentive for Russian specialists to respond to such recruitment efforts.

- Serving as a stepping stone to dismantlement opportunities: Collaboration on dangerous pathogens can help identify opportunities for joint dismantlement projects, another key CTR objective. Experienced researchers can provide guidance on the most effective use of facilities and on the removal or modification of research equipment no longer needed for military purposes. Research institutes also might provide introductions to other parts of the former BW complex, such as engineering and design facilities, where excess military-oriented equipment could be put to new types of peaceful use.

- Reconfiguring former Soviet BW-related activities: Severe cutbacks in funding for military programs have already led to a considerable redirection toward civilian activities of research and development that previously supported the Soviet BW program. However, large and diffuse research and development and standby production capabilities with BW potential remain in Russia. In the absence of alternative employment opportunities, defense scientists constitute a powerful lobby for maintaining facilities that are beyond Russia's national security requirements for defensive BW research. A substantial collaborative research program would provide new employment opportunities for many key scientists, thereby reducing pressures on the Russian government to invest in maintaining unnecessary facilities. Also, if such a collaborative program is designed to concentrate financial support at a limited number of the best Russian facilities, any weaker facilities–to the extent they remain viable–will have incentives to find work outside the area of dangerous pathogens, particularly in the private sector.

- Enhancing capabilities to combat bioterrorism: Both the United States and Russia are concerned about the growing threat of bioterrorism.[29] Expanded cooperation in basic research, epidemiology, diagnosis, and prophylaxis of diseases associated with dangerous pathogens can enhance the capabilities of both countries to identify and respond to emerging terrorist threats.

2. Public health benefits

- Improving understanding of the prevalence and characteristics of pathogens that pose threats to public health: The Soviet investment in BW-related research has resulted in a cadre of highly qualified scientists with unique knowledge about dangerous pathogens. Collaborative activity can provide the

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[27] Throughout this report the term defense scientists refers to scientists and engineers who participated in BW related activities before or after the disintegration of the Soviet Union in 1991. It is assumed that some defense scientists were engaged in activities prohibited by the 1972 Biological Weapons Convention and others were not. Unless otherwise stated, the emphasis in cooperation is on engaging those defense scientists who were most directly involved in research and development of dangerous pathogens with biological weapons potential.

[28] Rimmington, op. cit., p. 96.

[29] The threat of bioterrorism was raised on a number of occasions by Russian participants at the committee's workshop in Petrovo-Dalnyee.

United States with new insights into research capabilities, laboratory techniques, and knowledge that may not currently be known outside Russia.

- Strengthening capabilities to prevent, diagnose, and treat outbreaks of infectious diseases: Both countries have substantial capabilities in epidemiology and public health for monitoring outbreaks of diseases. Linking national capabilities through expanded cooperation can enhance global surveillance and improve epidemiologic investigations and responses to outbreaks of diseases.
- Enhancing international communications concerning disease trends and outbreaks: Strengthened communications links among individual investigators, research institutions, and government agencies can improve the capabilities of both countries to anticipate and respond to outbreaks of diseases and provide mechanisms to determine the source of outbreaks.

3. Economic benefits

- Improving the stability of Russian research institutes by increasing the commercial viability of their research products: Defense scientists with BW expertise are more likely to continue working on projects with promising economic futures, both for their institutes and for themselves, than to remain in place if they are offered only low-paying tasks with little future or very short-term technical challenges with uncertain long-term security. Each research product that achieves commercial viability is also a small contribution to Russia's transition to a market economy. At the same time, the reality is that Russian institutes have had great difficulty finding international or domestic markets for their products or finding partners who can help locate such markets. Some of the projects included in the collaborative program should help a few Russian institutes become more competitive commercially by focusing new attention on the importance of high-quality prototypes, strong quality-control systems, and well-developed marketing and distribution systems. Cooperation will provide opportunities for access to U.S. business and marketing skills in these and other areas.
- Leveraging limited national financial and human resources to serve national security and public health interests: Coordinated research activities in both countries on dangerous pathogens that pose current and potential health risks to the world's populations offer opportunities to combine limited financial and human resources in combatting dangerous infectious diseases.
- Providing new opportunities for the U.S. private sector to become more active in Russia: The current level of U.S. private-sector involvement in Russia in the development of vaccines, diagnostic devices, or other commercial commodities in the biomedical field is very low. Cooperation can lead to better appreciation of the capabilities of Russian specialists and provide easier access to Russian expertise and facilities. Coupled with appropriate commitments to respect intellectual property rights, such developments can increase the interest of the U.S. business community in investment, licensing arrangements, and expanded trade.

4. Scientific benefits

- Enhancing the base of fundamental knowledge of pathogenesis: A collaborative effort that engages Russian and U.S. scientists in fundamental science will provide opportunities for exploring new research avenues.
- Increasing the international availability of research results: Most Russian scientists cannot afford to subscribe to Western journals or attend scientific meetings in the West. On the other hand, U.S. scientists have a limited appreciation of the past accomplishments of Russian investigators because of a lack of English-language reports of their scientific findings. The proposed program to engage key Russian specialists in joint projects should significantly increase the exchange of information and knowledge between the two countries.

The Need for Coordination of U.S. Government Efforts

The U.S. government supports a growing array of efforts involving defense scientists (see Table E-1). In addition to the CTR and ISTC programs discussed previously, there are related projects of the U.S. Department of Energy (DOE) Initiatives for Proliferation Prevention, National Aeronautics and Space Administration, National Institutes of Health (including the Fogarty International Center), Civilian Research and Development Foundation, U.S. Department of Agriculture, and DOE's Chemical/Biological Non-Proliferation Program. At the highest level, the Gore-Chernomyrdin Commission has considered a few related programs through its three committees on health, science and technology, and defense conversion. To date, these activities have involved only limited engagement with the personnel and facilities of the former Soviet BW complex, but interest in such engagement appears to be growing.

CTR and ISTC now have more than five years of experience working with the defense scientists of Russia, but other U.S. organizations do not have comparable experience. As other programs undertake research activities with former BW scientists, systematic coordination among related programs is exceedingly important so that national security objectives are considered fully and that tax and customs exemptions with the Russian government are utilized whenever possible.[30] President Clinton created a special position, at the rank of ambassador, with the responsibility of coordinating these cooperation or assistance efforts.[31] Effective use of this or an alternative coordination mechanism is essential to ensure that the substantial potential benefits of cooperation with the former Soviet BW complex are realized and the risks that collaborative research efforts could contribute to illegal activities are minimized.

THE BLUEPRINT FOR COOPERATION

This chapter has provided the context and rationale for U.S.-Russian cooperation involving specialists and facilities of the former Soviet BW complex. Chapter 2 describes the initial NAS experience with a number of pilot projects designed to test the feasibility of such collaborative arrangements, while developing plans for long-term cooperation. This experience provided the basis for the five-year *Pathogens Initiative* outlined in Chapter 3. Chapter 4 describes a model for a subsequent sustained program of cooperation encompassing activities across a wider range of work on dangerous pathogens.

The framework for bilateral activity recommended in this report in time could become a basis for expanded cooperation among a number of key countries. Ultimately, enhanced international security and global health can be achieved only through broadly based multinational networks incorporating many of the elements stressed in the *Pathogens Initiative*.

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[30] Representative Floyd Spence. Letter to the editor. Washington Post, July 7, 1997.

[31] White House. 1995. Memorandum for the heads of executive departments and agencies on charter for special adviser to the president, April 4.

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Establishing the Basis for Long-Term Cooperation

This chapter describes the activities of the committee during fiscal year (FY) 1997 to develop the basis for long-term collaboration involving defense scientists working on dangerous pathogens. Insights gained during consultations with a large number of Russian specialists and lessons learned during the initiation of six pilot projects at two key Russian facilities are discussed. Then a policy and program framework is suggested for carrying out more ambitious programs that build on successful experiences to date.

IMPORTANCE OF RUSSIAN PARTICIPATION IN JOINT PLANNING

During the fall of 1996 and the spring of 1997, the committee undertook a number of activities in Russia to assess the opportunities for a long-term program of cooperation between U.S. and Russian specialists with special expertise in the epidemiology, prophylaxis, diagnosis, and therapy of diseases associated with dangerous pathogens. These activities were particularly important in initial assessments of the benefits that could be anticipated from such cooperation, as well as the challenges and costs of establishing appropriate arrangements. The committee gave special attention to the participation of Russian specialists who had been involved in the former Soviet biological weapons (BW) program.

To involve Russian specialists at a very early stage in the development of recommendations for a cooperative program, two complementary approaches were used:

1. Consultations were held with a range of Russian officials, managers of research institutions, and research scientists. The topics of interest included the general character of a long-term cooperative program, the availability of specialists and facilities to carry out a program, and the likely results of cooperation. An important purpose of the consultations was to help ensure that the committee's assessments of the technical basis for cooperation were authoritative and that proposed activities were realistic. Also, because the support of a number of Russian organizations will be an essential aspect of such a long-term cooperative program, the involvement of Russian officials and specialists from the planning stages was intended to give them a sense of genuine partnership in program development.

2. Pilot projects were initiated at two Russian facilities. These six projects are providing experience in the practical aspects of conducting joint projects, with most of the research activity carried out in Russia (see Box E-1 and Appendix E). At the same time, they are producing research results that, in and of themselves, are important. Also, they are making timely contributions at the scientist-to-scientist level to provide insights about the capabilities of the two countries in carrying out research on dangerous pathogens—insights that are critical for sustaining a broadly based long-term program of cooperation. Finally, funding by the Defense Department of the pilot projects recommended by the committee helped convince Russian colleagues that the committee's undertaking was a serious endeavor with strong backing from the U.S. government, thereby encouraging them to participate actively in planning the long-term program.

With this two-track approach, the committee quickly engaged a number of important Russian officials and defense scientists in its activities.

PLANNING FOR SUSTAINED COOPERATION IN THE LONG-TERM

The development of recommendations for long-term cooperation involved consultations with Russian colleagues through a variety of venues. Nine U.S. and sixteen Russian specialists took part in a roundtable hosted by Biopreparat in the Moscow suburb of Petrovo-Dalnyee in April 1997 to consider the general framework for cooperation. Specialists from Biopreparat and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) joined public health-oriented researchers and other specialists to discuss the organizational framework, financial aspects, technical dimensions, and research themes for a cooperative program. A joint summary of the conclusions of the meeting can be found in Appendix G.

Discussions continued at a smaller follow-up meeting organized by the NAS committee in Moscow in June 1997, attended by representatives of Biopreparat and directors of several of its key research institutes. This meeting brought into sharper focus future project directions and approaches for joint planning and development of specific research activities. At that time, Biopreparat informed the committee that it was organizing a Russian working group to serve as the point of contact for future discussions of bilateral cooperation, with the invited membership listed in Box 2-1. If all invited members of the working group choose to participate, it will have an excellent composition for this purpose.

Box 2-1 The following organizations have been invited by Biopreparat to form the working group for future discussion of bilateral cooperation:

- Biopreparat
- President's Committee for Conventional Problems of Chemical and Biological Weapons
- Ministry of Defense
- Ministry of Health
- Ministry of Science and Technology
- Russian Academy of Sciences
- Russian Academy of Medical Sciences

Individual institutes invited include the following

- State Research Center for Virology and Biotechnology, "Vector" (Koltsovo)
- State Research Center for Applied Microbiology (Obolensk)
- Institute of Immunology (Lyubuchany)
- Institute for Biological Scientific Instrumentation (Moscow)
- Plague Research Institute, "Microb" (Saratov)
- Central Scientific Research Institute for Epidemiology (Moscow)

NOTE: Biopreparat officials have indicated that other organizations will be involved as appropriate.

The National Academy of Sciences (NAS) and International Science and Technology Center (ISTC) sponsored an international symposium in the Kirov region in June 1997, with ISTC taking the lead in the organization: 30 Russian scientists, joined by 14 American, 6 Japanese, and 3 European specialists, covered a wide range of topics of broad interest. Some of the Russian participants presented specific project proposals.

A number of biotechnology activities and facilities previously associated with the former Soviet BW program are located in and near Kirov, which is 1,000 km east of Moscow. The symposium and subsequent visits to various organizations in Kirov provided opportunities for initial discussions with local specialists and with experts from other parts of Russia about future cooperation. A brief report prepared at the meeting and a list of attendees are included in Appendix H. The facilities visited are listed in Appendix C.

In addition to the organized meetings and visits, committee members participated in a number of

informal discussions with Russian organizations and individual specialists, beginning in November 1996 and continuing into the summer of 1997. Among the most useful discussions were conversations between committee members and Russian scientists during visits to the Russian institutes where pilot projects have been established.

The comments of Russian colleagues underscored the importance of high-level support for a long-term program by the Russian government. Several Russian colleagues informed the Russian Defense Council of NAS interest in expanding bilateral cooperation, and Biopreparat representatives subsequently advised the committee that the council strongly supported the initiative.

Overall, interactions between committee members and Russian specialists provided valuable insights into Russian capabilities and activities. Russian colleagues were very sensitive to both national security considerations (e.g., maintaining security for pathogen strain banks and sensitive research findings that could be misused by terrorist groups) and scientific opportunities, and they offered many useful suggestions about future cooperation. They also indicated strong support for the types of recommendations included in this report.

An important exception to the success of these consultations, however, was the refusal of the Russian Ministry of Defense (MOD) to participate in discussions of cooperation. Biopreparat and other Russian officials offered two explanations for this reluctance. First, for political reasons the difficulties encountered in the trilateral discussions on BW-related issues made MOD unwilling to become involved in cooperative activities of interest to the committee. Second, MOD was undergoing a major reorganization and was initiating a substantial reduction in the size of the Russian armed forces; therefore, MOD officials were not in a position at that time to discuss international cooperation. Consequently, the committee received no direct indications of MOD views on future cooperation. However, in 1996, MOD and its research institutes participated actively in an ISTC-sponsored international workshop in Pokrov, northeast of Moscow, which indicated some flexibility in the long-standing policy of keeping laboratories isolated from foreign contacts. Also, in Kirov, committee members and staff met with representatives of several civilian organizations that involve specialists from the MOD research institute located in the city in their activities. These Russian colleagues appeared optimistic that in the future the institute will become interested in international cooperation. The Biopreparat invitation to MOD to participate in the working group, as indicated in Box 2-1, is also of interest.

Should MOD remain reluctant to participate in bilateral endeavors, a number of key Russian personnel and several very important facilities would not be involved in the *Pathogens Initiative* discussed in Chapter 3. However, the Biopreparat complex provided much of the critical research and development support for the Soviet program; thus, the committee has concluded that Biopreparat is sufficiently important to warrant a *Pathogens Initiative*. Effective bilateral cooperation with specialists from Biopreparat institutions, supplemented by specialists from institutes subordinate to other Russian organizations, would be a significant contribution to reducing the likelihood of proliferation and expanding research that supports public health goals.

INITIAL PILOT PROJECTS

With Russian colleagues, the committee developed the cooperative pilot projects at two Russian institutes that are identified in Box E-1 and described in more detail in Appendix I. DOD provided financial support of about $420,000 to the institutes and an additional $80,000 to U.S. collaborators to support travel and related expenses. The first six projects began in June 1997 and are scheduled for completion by September 1998. In July 1997, DOD transferred funds for the projects to the ISTC for prompt disbursal to Russian participants.

Encouraged by the progress achieved in implementing the six projects, DOD subsequently

indicated a readiness to consider additional pilot projects; the committee then selected two more proposals prepared by Russian investigators that it considered interesting. These proposed projects, which are also included in Box E-1, are currently being processed by the ISTC.

With regard to the goals of the pilot projects set forth earlier, the decision to fund six projects at the beginning of the study proved sound for several reasons:

- Lessons learned about the roles of Russian ministries and institutions and of the parties to the ISTC in the development, approval, and implementation of these projects have been important in formulating the recommendations in this report. Also, the projects provide a base of experience that can assist in designing and implementing more ambitious projects.
- The projects provide an opportunity for U.S. and Russian scientists to establish personal contacts that will help sustain and expand research relations.
- The research topics are of considerable interest in Russia and the United States with regard to both scientific advancement and practical applications. Ties to health authorities and to industry, as well as to scientific institutions, are an important aspect of some of the projects.
- The projects test the practical aspects of transparency, with scientist-to-scientist contacts playing a significant role in this regard. Transparency is important for providing increased assurance that joint work on dangerous pathogens is not being misused to provide technical contributions to illegitimate BW-related activities.
- Reciprocal access to laboratories within the context of these projects offers new insights about biotechnology activities in key Russian facilities—an important contribution to confidence building.

Selection of the Institutes

Given the short lead time available for establishing these projects, the NAS committee, with DOD concurrence, decided to locate them at the State Research Center for Applied Microbiology in Obolensk and the State Research Center for Virology and Biotechnology, "Vector" in Koltsovo. This decision was based on the following considerations:

- As a result of the important roles the two institutes played in the BW program of the former Soviet Union, they have some of the strongest research capabilities related to dangerous pathogens in the country.
- These institutes have strong linkages with other institutes of the Biopreparat complex, institutes of MOD, and other institutes with capabilities related to dangerous pathogens. Therefore, they provide good initial points of entry in the development of a program of national scope.
- Through previous NAS activities in Russia, committee members were personally acquainted with the directors and other personnel of the two institutes and believed that they would be receptive to projects involving active bilateral collaborators.
- ISTC had been successful in initiating a few projects at the two institutes, beginning in 1994, which indicated that these institutes were prepared to overcome administrative hurdles in developing cooperative activities and would agree to provide access to their facilities.

In short, the two institutes are important in terms of their capabilities, experience, and organizational links to the former Soviet BW complex and to public health. In addition, they were ready to quickly initiate projects involving U.S. collaborators.

Selection of the Initial Projects

In late 1996, small teams of committee members and staff visited Obolensk and Koltsovo, where they reviewed proposals and consulted with leaders of the institutes and principal investigators of

proposed projects. They also made preliminary assessments of some capabilities of the institutes. These teams developed their project recommendations, taking into account the constraints of limited funds and the need to complete the projects by September 1998.

Obtaining early experience that would be useful in developing the long-term program was an important purpose of the projects. Thus, it was desirable to have the projects operational as soon as possible. This requirement meant that Russian institutes needed to have formal government approvals in hand or that this approval could be obtained easily. Therefore, a number of promising but yet-to-be-approved proposals prepared by the institutes were excluded from consideration because a delay of several months could be anticipated for both scientific and security reviews in Moscow. The committee recommends that some of these proposals be given priority for consideration in the *Pathogens Initiative*. However, the committee also strongly recommends that U.S. participants adopt a more proactive role in identifying possible topics and proposals for funding under the initiative now that the time constraints of the past year are diminished.

The committee approved the recommendations of its members who had visited the institutes and developed the following criteria for project selection during the course of its deliberations:

- Importance of the topic: the project will make an important contribution to the epidemiology, prevention, diagnosis, or therapy of any disease that is associated with dangerous pathogen(s) or that is (1) historically linked with BW applications or (2) a source of substantial public health concern. If successful, the project will open up a new area of important research on dangerous pathogens.
- Quality of the proposal: the project is scientifically and technically sound; anticipated results are clear; the project is feasible; there is a strong work plan; budget and manpower estimates are appropriate; and there are measurable milestones.
- Quality or capacity of the principal investigator, research team, and facilities: the proposing laboratory must have strong technical capabilities in the general research area, and the personnel and facilities proposed must have adequate capabilities to carry out the project.
- Provision for strong U.S. collaboration: the project involves a topic that will attract strong and relevant U.S. expertise, and the commitment of the U.S. collaborator(s) is clear.
- Engagement of former Soviet BW expertise: the project involves former or current defense scientists, or facilities or it provides important contributions to a larger program that involves such scientists or facilities.
- Promotion of transparency: the project meets standard ISTC access criteria, and reciprocal laboratory visits between collaborators are an integral aspect. Projects that meet such criteria and also offer access to facilities or personnel not previously engaged in collaborative projects are of particular interest.

The selected projects scored high when measured by the foregoing criteria. Also, in considering these and other aspects of each project, the committee made the judgment that the project's potential contributions to public health or U.S. national security interests outweighed the potential risk that it might contribute to the development or improvement of offensive BW capabilities.

Use of the ISTC Mechanism

The committee decided that the ISTC was the best mechanism to use for entering into agreements with the Russian institutes and for transferring funds to them. Because the objectives of the initial projects were entirely consistent with its purpose, the ISTC formally accepted NAS as one of its

partners. This status enabled the Academy to use well-established and reliable international mechanisms to develop and implement the projects.[1]

Reliance on the ISTC solved many problems encountered in supporting research activities in Russia, including issues of foreign access to project sites, sharing of intellectual property rights, allowable costs, financial auditing, reporting requirements, overhead charges, wage scales, and exemptions from taxes and customs fees. In all of these areas, NAS adopted standard ISTC approaches that were also fully acceptable to the two Russian institutes and to the U.S. and Russian governments. Of special importance is the ISTC procedure of providing funds for salaries directly to individual researchers, thereby circumventing opportunities for intermediaries to divert a portion of these funds.

The committee now feels even more strongly about the correctness of its decision to use the ISTC mechanism in light of reports that some U.S. agencies have employed other mechanisms that lack special waivers associated with handling funds for scientific research and, as a result, have lost up to 50 percent of their funding to Russian tax collection and pension accounts.[2] Perhaps a broadly based bilateral agreement between the two countries can address these issues, but in the absence of such an agreement the ISTC remains an important institution for facilitating joint projects.

Value Added by the NAS Committee

In working with ISTC staff and reviewing related ISTC projects, the committee recognized that it could offer value added to the usual approach of the ISTC. In general, the governments that are parties to the ISTC agreement have had little influence over the proposals related to dangerous pathogens that Russian institutes have chosen to submit for consideration; they have simply considered any proposals that are submitted to the ISTC. These governments have then searched for appropriate collaborators for the most interesting proposals, relying on the collaborators to obtain their own funds for active participation in the projects.

Value added by the NAS was reflected in the following:

- U.S. specialists selected by the Academy were involved not only in choosing the research topics to be developed into fundable proposals but also in modifying the research plans. Therefore, the NAS was in a strong position to ensure that proposals were oriented toward priority scientific interests of the United States as well as toward Russian interests. Also, the early involvement of U.S. specialists improved the quality of the proposals submitted for approval to both the committee and the U.S. government as an ISTC party.
- The committee includes leading U.S. scientists in the fields of interest, with experience in research directly related to biological defense. Therefore, it was in a good position to critically review not only technical merit but also linkages to BW, including the potential contribution of research projects to offensive BW capabilities.
- In view of the committee's extensive connections with the U.S. research community, it was able to enlist U.S. collaborators who are well qualified for the tasks and, recognizing the direct benefits of collaboration, highly motivated to work closely with the Russian teams throughout the lifetimes of the projects.

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[1] In 1996 the parties to the ISTC decided to encourage other government and nongovernment organizations with access to financial resources to use its legal, management, and financial frameworks for developing and implementing projects that are consistent with ISTC objectives. The U.S. government recommended that the ISTC accept NAS as a partner for supporting cooperative activities directed to dangerous pathogens. Projects proposed by the Academy are thus subject to the review and approval of the U.S., Japanese, and Russian governments and the European Union during ISTC deliberations.

[2] See Lelyveld, M. S. 1997. Skimming Cuts Aid to Russian Scientists. *Journal of Commerce* May 13.

- The committee and staff have extensive experience in developing and reviewing proposals and are skilled in translating Russian concepts into proposal language that is easily understandable in the West. Thus, they were able to substantially reduce the lengthy development time required for most ISTC projects. The usual time needed to launch an ISTC project includes 6 to 12 months to develop a fundable proposal and an additional 6 to 9 months from ISTC acceptance of a fundable proposal until the operative commencement date of the project—a total of 12 to 21 months. The required time to launch the six pilot projects included three months for the Russian institutes to prepare fundable proposals and three months from the date of submission to ISTC until the operative commencement dates.

INSIGHTS FROM THE PILOT PROJECTS

Although the pilot projects are still in the early stages of implementation, a few lessons have been learned in developing them that are important in considering future activities.

- Despite the loss of hundreds of scientists and decline in the quality of laboratories and equipment, each of the two Russian institutes retains a few hundred skilled scientists and strong capabilities to conduct important research. The State Research Center for Virology and Biotechnology has a larger staff and more diverse facilities than the State Research Center for Applied Microbiology.
- As of June 1997, the two institutes had more than 100 unfunded proposals of highly variable quality. Some had been submitted to funding agencies in Russia and abroad, and others were still in the institutes awaiting indications of even minimal interest from funding sources. Although some proposals appear attractive for cooperative research efforts, a number of the most interesting ones involving dangerous pathogens still require formal approval of the Russian government, which may take three to six months or longer.
- The institutes have only limited e-mail capabilities and do not have regular access to the World Wide Web.
- The institutes attach great importance to having active U.S. collaborators working on their projects. In addition to benefiting from collaboration during the projects, institute leaders believe that foreign collaborators can assist in securing funds to expand projects into related areas of interest to the institutes. Effective collaborators have been the exception rather than the rule, however, with foreign-funded projects at the institutes.
- The institutes consider the ISTC the best mechanism for distributing foreign funds within Russia. As previously noted, some U.S. experiences with other mechanisms have been less satisfactory for a variety of reasons, such as loss of funds to central offices in Moscow, customs problems, and taxes imposed at the local level. At the same time, sending equipment, supplies, and samples from abroad to research institutes in Russia, even through ISTC channels, will be complicated.
- Although the two institutes have long-standing ties with institutes of the MOD and other institutes in the civilian sector, they seldom propose multi-institute projects for foreign financing, because this adds to administrative complications. In particular, MOD has not yet been involved in research projects that require giving foreign collaborators access to research laboratories at military facilities.

As the pilot projects proceed, other insights undoubtedly will be gained. The hands-on experiences of U.S. and Russian collaborators will be of special interest, in both hosting colleagues and working in the laboratory facilities of those colleagues.

PRINCIPLES TO GUIDE BILATERAL COOPERATION

Based on the committee's consultations with Russian colleagues and the experience gained in the pilot projects, three overarching principles were developed to guide future bilateral activities directed toward dangerous pathogens. These principles also appear relevant to other cooperative programs that engage specialists from the former Soviet BW complex. Broad acceptance of such principles will reduce confusion in Washington and Moscow about approaches that are appropriate in this sensitive area and will help ensure that approaches used in different programs are mutually reinforcing.

1. Projects should be collaborative in design and conduct.

- Only projects that are of interest to specialists in both countries should be undertaken. There are not sufficient funds to support all activities proposed, and an important criterion for project selection is the level of support among specialists in both countries for pursuing the proposed activities. A measure of this interest is the extent of collaboration included in the implementation of a project.
- All projects should be conducted on the basis of cooperation, not assistance, with each side making intellectual, financial, and in-kind contributions. Carrying out projects that are designed as part of foreign assistance activities, or are perceived as such could lead to misconceptions that limit political support for such activities. Further, both countries have much to contribute, and although the Russian contribution may be largely intellectual at this time, this intellectual resource warrants the label of cooperation on projects.
- All relevant constituencies in both countries should be able to apply for participation in the program. Bilateral programs will never be large enough to include all interested and important U.S. and Russian specialists. However, the individual activities should be as encompassing as possible, and competition for financial support should be open to all qualified specialists.

2. Projects should be designed and conducted in a way that maximizes transparency.

- Activities should be carried out in an environment of openness. Free exchange of information between participants in cooperative activities is central to achieving both scientific and national security objectives. Transparency begins at the project level and should be based on regular and sustained contacts between U.S. researchers and their Russian counterparts and on regular visits to facilities where the research is carried out. In this regard the ISTC has developed guidelines for access to facilities at the project level (Box 1-2). Although limited, these guidelines are a good initial basis for cooperation. In time, the broader concept of transparency described in Chapter 1 should encompass a wider range of research activities at the institute level.
- Direct contacts among specialists should be stressed. Given the sensitivity of the topic, government officials in both countries should be involved in the development and approval of projects. However, once a program has demonstrated that it will be managed responsibly, governments should minimize interference. In short, they should be promoters of responsible cooperation but should give the cooperating scientists maximum flexibility once the ground rules for cooperation have been established.
- A central coordination point in each government should be apprised of anticipated cooperative activities. Given the increasing number of bilateral efforts, it is essential for central offices to have up-to-date information on such activities. Because the same scientists may be participating in projects under the auspices of different cooperative programs, such a registry will be most useful if it includes all cooperative activities involving defense scientists.

3. Results of cooperative projects should be disseminated to the widest possible interested audience.

- Whenever possible, research results should be promptly published or made available to international audiences through other channels. A critical aspect of international science is sharing project results. Prompt and broad distribution of findings should have beneficial effects in encouraging

reciprocal sharing of information that helps prevent the unnecessary duplication of research activities while broadening transparency.

- Intellectual property and sensitive findings should be protected. Notwithstanding the desirability of wide dissemination of research results, scientists working with dangerous pathogens that have BW potential have a special responsibility to ensure that, in accordance with the Biological Weapons Convention, sensitive information is not disseminated to irresponsible parties. Also, researchers should be able to protect information that has commercial value. Mechanisms should be developed to help ensure an appropriate balance between the free flow of scientific information and limitations based on these two legitimate reasons for restricting the dissemination of information in certain cases.
- Intellectual property rights resulting from cooperative activities should be shared by the participating institutions on fair and equitable terms. As cooperative projects develop, mutual confidence that project collaborators will not misuse intellectual property should increase; to this end, project agreements should include appropriate provisions for the rights to such intellectual property. The provisions of the ISTC model project agreement set forth in Box 2-2 provide a point of departure for considering arrangements for specific projects.

Box 2-2 Highlights of ISTC Provisions on Intellectual Property Rights

- All rights to research results reside with the Russian institution that carries out a project.
- All ISTC parties are entitled to no-cost licenses to use research results for noncommercial purposes.
- The financing party is entitled to a no-cost exclusive license to use research results for commercial purposes in its territory.
- The Russian institution may use research results for commercial purposes in other areas of the world or may be compensated for licenses for such use.
- The financing party and the Russian institution may agree on alternative arrangements.

Source: ISTC Statute, Article XIII, March 17, 1994.

ORGANIZING RESEARCH ACTIVITIES IN THE FUTURE

Critical aspects of near-term cooperation will be the criteria used to select the most promising joint projects, the size and scope of individual projects, and the financial arrangements for supporting the projects.

Criteria for Judging Research Proposals

The criteria developed during assessments of the pilot projects and set forth previously in this chapter are appropriate for evaluating the merits of future projects. The following two criteria are also important if an expanded program is initiated:

1. Likelihood of sustainability: the project should be of interest to commercial, government, or other organizations that want to build on the research results and have the financial means to continue supporting research in the general field after project completion. Many aspects of research on dangerous pathogens are considered to be within the public health responsibilities of governments; therefore public funds are undoubtedly needed to continue activities in a number of areas. However, in some areas such as diagnostic devices and vaccines, efforts to interest commercial organizations in providing financial support are essential.

2. Promotion of linkages between defense scientists or facilities and civilian scientists or facilities: new internal networks should be reflected in project activities. Although defense scientists are very capable, some civilian institutions have more extensive experience and official responsibilities in addressing public health problems. In some cases, multi-institutional projects involving specialists from

both communities may be appropriate; in other cases, complementary projects may be the preferred course. In either case, joint planning and coordination activities should contribute to project success and bring the two communities closer together.

Size and Scope of Research Projects

In general, future projects should be larger and longer in duration than the pilot projects. The ISTC has had quite positive experience in supporting larger projects that reflect the importance of keeping research teams together. Also, establishing large numbers of small projects entails high administrative costs. Three-year projects involving teams of about 10 Russian specialists appear to be appropriate. At the same time, flexibility for supporting smaller or larger projects, depending on specific research objectives, is important.

Financial Realities

Each side should cover its own expenses associated with cooperation to the extent possible, with equal sharing of all costs as the long-term objective. Given current financial difficulties in Russia and the fact that monetary support is only one type of contribution to a collaborative project, the following approach for covering costs of collaboration in the near term appears appropriate:

1. For cooperative research projects,
   - The United States should cover costs in the United States; and
   - The United States should contribute to costs in Russia in accordance with ISTC regulations about allowable costs (e.g., salaries; equipment; supplies; travel; and technician, computing, and support costs unique to the project) and should pay the expenses of U.S. collaborators in Russia, with Russia covering other facility, administrative, and indirect costs.
2. For technical meetings and workshops in Russia,
   - The United States should cover the expenses of U.S. participants;
   - Russia should cover the expenses of Russian participants; and
   - Both should share additional costs associated with events.
3. For technical meetings and workshops in the United States,
   - Russia should cover the costs of international travel; and
   - The United States should cover all other costs.

A GOOD BASIS FOR FUTURE COOPERATION

The activities of this committee, together with related efforts of U.S. agencies, have generated considerable interest and growing support in Russia among the community of former and current defense scientists in joint projects with U.S. specialists directed to the biological sciences and biotechnology. Joint projects directed to dangerous pathogens should be an important subset of such cooperation.

With the transfer to Russian institutes and U.S. collaborators of approximately $500,000, six pilot projects are under way; two others are in the final stages of development. The process of developing these projects and their first few months of activity are demonstrating that collaborative efforts operated under expert guidance and within an effective administrative framework can engage key Russian defense scientists, attract excellent U.S. partners in academia and government, and support joint work on high-priority topics with the potential to achieve significant benefits.

In addition to the costs of supporting research activities at the two Russian institutes and the travel and related expenses of U.S. collaborators, significant costs have been incurred in developing the

pilot projects and in establishing the base for future cooperation, including joint planning activities with Russian colleagues. However, the percentage of total funds devoted to such supporting activities will decrease sharply if an expanded cooperative program is pursued, as set forth in Chapter 3.

In summary, the recent experience of the committee confirms that despite current political uncertainties and economic difficulties in Russia, it is feasible to implement important cooperative programs involving Russian defense scientists that serve the national security, public health, economic development, and scientific objectives of both countries as set forth in Chapter 1.

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Phase 1: A *Pathogens Initiative* to Expand Cooperation

A WINDOW OF OPPORTUNITY FOR INITIATING JOINT EFFORTS

The recent activities initiated by the National Academy of Sciences (NAS) in Russia and discussed in Chapter 2 have helped open a window of opportunity for engaging significant elements of the former Soviet biological weapons (BW) community in joint projects of public health significance directed to dangerous pathogens. As evidenced by the major time commitments of key Russian specialists in working with the NAS committee and staff, Russian officials and scientists are clearly interested in expanding cooperative endeavors in the near future.

Meanwhile, ISTC support of projects at Biopreparat research institutes is increasing, and the Department of Energy (DOE) recently announced a new program for supporting former Soviet BW specialists under the auspices of the Initiatives for Proliferation Prevention (IPP). These developments have added to the desires of the Russian scientific community for expanded cooperation that includes infusions of financial resources from abroad.

Russian readiness to expand cooperation involving one of the most sensitive components of the former Soviet military establishment can be attributed to a variety of other developments as well, including the following:

- As Biopreparat seeks new roles for providing services to the Ministry of Health and producing items for the civilian market, its research institutes–after favorable initial experiences with the International Science and Technology Center (ISTC) projects and limited success with foreign companies–are increasingly interested in participating in public health efforts with foreign partners.
- Many Russian nuclear research institutes and production enterprises have participated effectively in international programs, including organizations that have been involved in sensitive activities; leaders of the biological defense community are interested in establishing analogous international programs.
- The Ministry for Science and Technology has assumed increasing responsibility for financing and approving civilian activities at institutes that, in Soviet times, were involved in BW-related research; the ministry's interest in the benefits of international cooperation is well known throughout the Russian scientific community.
- The autonomy of political leaders is increasing in regions of Russia where research and related facilities involved in former Soviet BW efforts are located. Most regional leaders want to capitalize on the advanced technological capabilities of such facilities to promote educational opportunities and economic growth. It is likely that a number of regional governors recognize the importance of foreign partnerships in achieving this goal. As one example, the Communist governor of the Kirov region indicated to committee members a readiness to encourage such cooperation in biotechnology.
- In government agencies in Moscow and at some research institutes, international cooperation, including scientific cooperation, in combating bioterrorism that could strike Russia is a topic of increasing interest.

As noted previously, resistance to international cooperation persists within the Ministry of Defense (MOD). However, MOD apparently has not objected to Biopreparat's outreach, and some well-informed Russian colleagues believe that in the future, MOD will allow its institutes to join in cooperative efforts. Also, the interest of the Russian Defense Council in promoting cooperation and its reported endorsement of the NAS activity are encouraging.

Biopreparat institutes and enterprises were a major component of the former Soviet BW complex. Effective engagement of Biopreparat specialists and institutes therefore warrants a substantial bilateral effort even if MOD remains reluctant to participate.

Although Russian interest in cooperation is increasing, the future political course within Russia remains difficult to predict, and curtailment of bilateral cooperation with the United States in sensitive areas could be among the early targets if a reversal of the current movement toward political and economic reform occurs. As cooperation becomes more ingrained in the scientific community, joint efforts are more likely to survive severe political shocks, which underscores the importance of establishing and broadening such cooperation as soon as possible.

In view of the foregoing considerations, the committee believes that prompt action to follow up on recent steps toward expanded bilateral cooperation is very important.

RECOMMENDATION FOR A *PATHOGENS INITIATIVE*

Drawing on its positive experiences during 1996 and 1997 and current Russian interest in expanding cooperation, the committee recommends that a *Pathogens Initiative* focused on the public health aspects of dangerous pathogens begin as soon as possible. It will substantially expand the initial program of pilot projects described in Chapter 2 and will build on the limited efforts of several U.S. government agencies in this specialized field as presented in Table E-1.

If the Department of Defense (DOD) decides to support a *Pathogens Initiative*, as recommended in this report, the program will provide significant civilian research opportunities for defense scientists. The assurance of regular paychecks will reduce the economic incentives for these scientists to look elsewhere for financial support, including states of proliferation concern. Thus, the program will directly support DOD's mission to prevent diffusion of critical technical know-how that could assist in developing BW capabilities.

The core of a *Pathogens Initiative* should be joint research projects directed to the epidemiology, prophylaxis, diagnosis, and therapy of diseases associated with dangerous pathogens, as well as related fundamental research. The approaches for selecting and administering such projects developed during the implementation of pilot projects, described in Chapter 2, should serve as the initial framework for an expanded research program.

The *Pathogens Initiative* is projected to last five years, beginning in fiscal year (FY) 1998. The research and other components involved are discussed below. As the program matures, additional activities may be included and some recommended activities and approaches may be modified to reflect the experience gained.

If successful, the *Pathogens Initiative* should lead quite naturally to a state of sustained, transparent cooperation with Russia. This cooperation should be at a level of activity that provides attractive opportunities for a significant number of specialists from each country while at the same time concentrating research at a limited number of high-quality facilities in Russia. A favorable political environment is necessary, and the joint efforts envisaged should, in turn, contribute to improved bilateral political relationships. A possible template for sustained cooperation as a follow-up development to the *Pathogens Initiative* is presented in Chapter 4.

Organizational Structure

If a *Pathogens Initiative* is undertaken, the topic of expanded bilateral cooperation directed toward dangerous pathogens should be considered and endorsed at the intergovernmental level at an early date.

When the committee began discussing cooperation with Russian colleagues during the fall of 1996, Russian officials and scientists advocated prompt consideration of the initiative by the Gore-Chernomyrdin Commission (GCC). They argued, in particular, that endorsement at the intergovernment level would strongly encourage MOD to become involved and would help resolve many of the policy, implementation, and budget issues confronting other participating Russian organizations.

The pilot projects did not appear to constitute a sufficiently robust program to warrant consideration at the GCC level during 1997. Also, these projects could be implemented quickly through the ISTC with little need for political endorsement at a higher level. However, an expanded program will raise the political as well as scientific stakes considerably, and intergovernment endorsement could be helpful in providing impetus for an expansion in addition to encouraging coordination among related bilateral efforts.

The committee believes that the strong support of both governments is important for successful implementation of a *Pathogens Initiative.* It recommends that the two governments provide political support for such a program through the GCC or through another appropriate intergovernmental mechanism.

In addition to obtaining intergovernment endorsement of the *Pathogens Initiative*, the U.S. government should support a well-qualified technical working group to meet regularly with the Russian working group established by Biopreparat in the spring of 1997 to interact with the committee. The two working groups could address many of the details of cooperation for presentation to both governments. The suggestions of the Russian working group thus far have been constructive and realistic. The initial membership of the Russian working group is set forth in Box 2-1.

A *Pathogens Initiative* also should be accompanied by a stronger mechanism within the U.S. government for coordinating technical programs that involve cooperation with former Soviet BW specialists, including joint research on dangerous pathogens. Several organizations—including the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Food and Drug Administration (FDA), and U.S. Department of Agriculture (USDA)—have special technical capabilities that should be combined with nongovernment scientific capabilities to provide a focal point for coordination of scientific and technical aspects of the program. This coordinating body could greatly facilitate coordination of the *Pathogens Initiative* with closely related activities carried out through other U.S. government channels such as the ISTC and IPP. Coordination of these activities should also extend to global programs of infectious disease prevention and control, such as the World Health Organization (WHO) Division of Emerging and Other Communicable Diseases, Surveillance and Control (EMC).

An important concern is the possibility of a downturn in U.S.-Russian relations that is so severe it requires the termination of cooperative efforts. If such a change came abruptly, little could be done to safeguard against possible diversion of Russian expertise to prohibited activities. However, if Russian performance of the project agreements became impossible, the U.S. could terminate the agreements with 30 days notice and retrieve unspent funds.

Research Collaboration

The lessons learned in selecting, developing, and implementing the six pilot projects serve as important building blocks for the program. In particular, they suggest important new directions for collaboration. For example, at the beginning of deliberations, the committee hesitated to become too deeply involved with pathogens that have been historic BW agents. However, as discussed in Chapter 1, it is now much clearer that investigations of pathogens with BW potential are not only feasible but desirable if the goal of mutual assurance that activities and intentions are consistent with international obligations is to be achieved. A number of leading specialists in both countries fully recognize the importance of transparency as key to preventing the dual-use issue from becoming a major impediment to such cooperation, and transparency assumes its rightful level of significance when applied to the pathogens of greatest concern.

The recommended research effort of the *Pathogens Initiative* involves 15 three-year joint projects initiated each year. This recommendation is based on the following considerations:

- Significant joint research activities should be located at the most important Russian institutions with research capabilities related to dangerous pathogens that were established in the framework of the Soviet BW program. (Although Boxes 1-2, 1-3, and 1-4 provide a list of candidate institutes, not all of them will compete successfully for joint projects.) This program should include MOD institutes when they are prepared to participate. It is estimated that from the pool of 45 active projects when the program is fully operational, an average of 3 projects will be located at each participating Russian institution. Following the pattern established during development of the pilot projects, teams of U.S. experts should visit all potential participating institutes of interest to ensure that their proposals are consistent with current capabilities.
- The 15 projects initiated each year could engage about 150 Russian researchers on a full-time basis over a period of three years, or a larger number if there are some part-time participants. Using the ISTC estimate of $10,000 to support one full-time Russian specialist in Russia per year (including salary, equipment and supplies, technician and administrative support personnel, travel, and limited overhead), the average three-year cost to the United States is estimated at $300,000 for each project. Because up to 45 projects will be active at any given time, more than 450 important Russian researchers will be participating, including a limited number of part-time participants (see Table E-2 for phasing of joint research projects). Such part-time participants will be contractually obligated to spend the remainder of their time on activities acceptable under the Biological Weapons Convention (BWC). According to Russian colleagues, more than 10,000 scientists are still associated with institutions of the former Soviet BW complex, with an estimated 1,500 having the high-level skills necessary to carry out work on dangerous pathogens.[1] Thus, the program will involve a substantial proportion of the leading specialists of interest. If all U.S. efforts in this field are well coordinated, joint projects could engage most of the leading defense scientists.
- The committee believes that the pool of U.S. specialists is sufficiently large that appropriate collaborators will be available to participate in a program of this size. Each U.S. collaborator will receive an average of $165,000 for the three-year period. It is assumed that one-half of the U.S. collaborators will host research visits of 3 to 12 months by Russian colleagues and one-half will send postdoctoral

[1] Well-informed senior Russian specialists advised the committee that of the 9,000 scientists in the Biopreparat complex; about 1,000 could be considered highly skilled senior researchers with considerable experience related to dangerous pathogens. Other well-informed Russian scientists stated that between 150 and 200 scientists are currently working on biological defense issues at MOD facilities. Still others contended that there are several hundred senior researchers at the plague institutes and other civilian facilities who previously conducted work related to dangerous pathogens with financial support from MOD.

scientists or graduate students to Russia for 3 to 6 months by drawing on these funds. The principal investigator and collaborator will also make exchange visits, and the funds will cover these costs as well as provide some salary and overhead reimbursement. Some projects will involve long-term exchanges in both directions, some will call for one-way long-term exchanges, and others will include only short-term exchanges of one to several weeks. In any event, the desirability of long-term exchanges involving serious side-by-side research is clear. Some U.S. institutions, such as USAMRIID and CDC, can provide collaborators for a limited number of projects. Other U.S. organizations, particularly universities, will serve as hosts for most of the projects. In this regard, a special effort is needed to ensure that the U.S. research and development community is aware of the *Pathogens Initiative* and that interested scientists from many institutions have the opportunity to apply to participate in the programs developed.

In short, focused joint research activities of this magnitude will make a substantial contribution to public health and national security and will concentrate research on dangerous pathogens at carefully selected facilities in each country.

Framework for the Effort

The committee recommends clustering collaborative research projects in the following seven program areas:

1. anthrax,
2. melioidosis and glanders,
3. plague,
4. orthopox viruses,
5. viral hemorrhagic fevers,
6. other dangerous pathogens and diseases of public health concern, and
7. cross-cutting basic research related to dangerous pathogens.

The first five areas are directed to important agents and diseases historically linked with BW activities. In each of these areas, Russian institutions are believed to have invested significant resources in research that has been largely unknown outside Russia.

The sixth program area will provide opportunities to address other pathogens and diseases of public health concern. Some pathogens of broad public health interest, such as *Francisella tularensis*, may be of BW concern, whereas others, such as those that cause tuberculosis and influenza, may not be historically associated with BW. This program area is particularly important in permitting key defense scientists who are interested in addressing problems unrelated to BW to participate. It will also expand the pool of potential U.S. collaborators beyond the limited number of scientists engaged in research on agents of BW concern. In addition, this area may increase the possibilities for commercially viable activities.

Similarly, the seventh program area provides additional opportunities for cooperation in fundamental research related to a variety of dangerous pathogens or diseases, with immunology being an example of an area of interest.

The committee's selection of these program areas followed consultations with Russian colleagues who provided assurances that these areas are of interest to Russia. They anticipate that if an expanded cooperative program is undertaken the concurrence of the Russian government about these specific areas will be forthcoming.

Russian colleagues have proposed that joint Russian-U.S. teams meet to develop comprehensive approaches for addressing pathogen-specific program areas. Their concept, set forth by representatives of Biopreparat during the June meeting in Moscow, is that each program area should include projects at several institutes concerned with epidemiology, studies of strain variations, identification and diagnostic techniques, prophylaxis and treatment techniques, and application of research findings. They have

suggested including within each program area a jointly agreed-upon list of candidate projects costing up to $5 million for the participating Russian institutions over a period of five years. They recognize that funds probably will not be available to support all proposed activities within the $5 million ceiling.

The committee considers the Russian proposal a good point of departure for further discussion of the scope and priorities of the pathogen-specific program areas. In addition to clarifying scope and priorities, joint teams should play a useful role in encouraging the development of specific proposals by institutions in both Russia and the United States that fit within the agreed-upon program frameworks.

Also, the joint teams should ensure that the Russian institutions being considered for participation in the program have the capability to provide and maintain laboratories at an adequate level. Many laboratories are currently in a state of disrepair and are frequently deprived of necessary power, water, and supporting services; substantial Russian investments are necessary if such laboratories are to be involved in the program. As previously noted, projects should be located only at facilities capable of carrying out the proposed activities; any rehabilitation of facilities is the financial responsibility of the institution proposing the project.

In any event, individual project proposals should be considered through appropriate review mechanisms in both countries on a project-by-project basis. Those that are most important, in accordance with the criteria set forth in Chapter 2, should receive funding first. There is no reason to divide available funds equally among the seven areas. Indeed, division of funds should depend largely on the quality of the project proposals in competition with each other across program areas.

Finally, the existing pilot projects should be incorporated into the program within the context of the program areas described. These projects were intended to provide early results on a limited scale and represent truncated versions of longer-term projects initially proposed by the Russian institutes. All received favorable evaluations, and some have good potential for long-term sustainability. Some or all of the projects may produce results that justify continuation beyond their scheduled termination dates in 1998.

Involving Additional Russian Institutions

If MOD indicates interest in participating in the program, the exploration of possible collaborative projects involving its institutes should receive high priority. The program also should be prepared to support MOD specialists working at Biopreparat institutes or as subcontractors to Biopreparat institutes if appropriate projects are proposed.

Several Biopreparat research institutes, in addition to the two that are carrying out pilot projects, have significant capabilities and should become involved in the program. For example, the Institute of Immunology in Lyubuchany, the Institute for Highly Pure Biopreparations in St. Petersburg, and the Institute for Scientific Biological Instrumentation in Moscow are believed to have strong capabilities and have expressed interest in collaborative projects; they may be considered early candidates for projects. Other institutes are identified in Boxes 1-2, 1-3, and 1-4.

The possibility of including Russian engineers and technical personnel who played key roles in designing the processes and equipment used in the former Soviet BW program should be explored. Their involvement in collaborative activities could help open opportunities for joint efforts to reconfigure former BW facilities under the Cooperative Threat Reduction (CTR) program. Alternatively, such technical personnel may be more appropriate participants for other U.S.-sponsored programs, such as the IPP. The *Pathogens Initiative* could provide brokering services for U.S. programs that do not have comparable contacts within the Biopreparat establishment. In this regard, Biopreparat facilities at Omutninsk, Pokrov, and Berdsk and engineering research institutes in Moscow and Kirov have indicated interest in collaborative activities; their scientific and engineering potential deserves careful attention.

A special opportunity to engage previously isolated specialists from Biopreparat and MOD facilities may exist in Kirov. The recently established Volgo-Vyatka Applied Biotechnology Center, which served as host for the international symposium in the Kirov region in June 1997, is well positioned to provide introductions to several important MOD and Biopreparat institutions in the region. Also, Biotin, a major Biopreparat biochemical production enterprise with extensive contacts in the region, has indicated an interest in joint projects. A follow-up visit to Kirov in the near future may be a useful step toward broadening Russian participation in the *Pathogens Initiative* and related engineering efforts.

The Plague Research Institutes in Saratov and Stavropol have indicated interest in participating in cooperative activities, and on-site visits by U.S. experts are needed to carefully assess their capabilities. At a later date, assessments of the capabilities of the three other plague research institutes in Russia also should be considered.

Finally, as suggested in previous chapters, efforts should be considered to link former Soviet BW facilities and civilian institutes in common projects. There are a number of well-known civilian institutes with relevant research interests in the Ministry of Health, the Russian Academy of Medical Sciences, the Russian Academy of Sciences, and the Russian Academy of Agricultural Sciences; they should be encouraged to cooperate with former Soviet BW facilities as appropriate. Although the past capabilities of most of the civilian institutes are well known in the West, visits to these institutes are needed to better appreciate their current capabilities after extensive losses of personnel and aging of equipment.

Supporting Activities

Improvement of the electronic communications capabilities of Russian institutions participating in joint projects is important for meaningful international collaboration. Communications upgrades for Russian participants can be built into large projects or clusters of small projects at the same location. Installation costs of such upgrades depend on the specific institution and could range from thousands of dollars for computers, modems, and links to local telephone circuits to hundreds of thousands of dollars for satellite facilities at remote locations such as Koltsovo. Operating expenses also must be considered because e-mail and Internet services can be costly for impoverished institutions. Given the importance of this topic and the specialized nature of an authoritative assessment of needs, early joint assessment of electronic communications capabilities within the Biopreparat complex by well-qualified experts is important. The primary focus should be on institutes with strong potential for participating in sustained collaborative efforts.

In yet another area, both the Saratov Plague Institute and the Ivanovsky Institute for Virology have proposed projects for upgrading the safekeeping and utility of their strain collections, which serve as standards for the country. The Gamaleya Institute of Epidemiology and Microbiology also has national reference collections of strains, and the Chumakov Institute for Poliomyelitis and Viral Encephalitides holds a reference collection in its field. A number of other institutes have specialized collections. Russian institutes with standard reference collections or other significant collections should be encouraged to prepare project proposals for more effective utilization and maintenance of the strains; those that receive high evaluations should be considered for support. An important aspect of collaborative projects concerning pathogenic strains should be the procedures that are in place or that will be adopted to ensure transparency about how these strains are to be used. Such transparency should help ensure that the projects undertaken not contribute to activities that violate international obligations pursuant to the BWC. Although Russia has many regulations governing the handling and use of strains, the details of such regulations are not widely known outside the country. A comparison of recently promulgated U.S. and Russian regulations should be considered as a topic for a workshop or a joint project.

Finally, exchanges of information about the biosafety regulatory frameworks for handling dangerous pathogens in the two countries began during initial consultations with Russian colleagues. Box

3-1 lists some of the relevant Russian laws and regulations. Because such regulations are still evolving in both countries, periodic reviews should be held of requirements that could impinge on cooperative programs. Of particular interest would be early workshops to consider the following issues: registration of high-hazard laboratories, control over collections of strains of dangerous pathogens, setting and monitoring standards biosafety, and procedures for controlling the movement of dangerous pathogens within a country and between countries.

Box 3-1 Selected Russian Laws, Decrees, and Regulations on the Control of Dangerous Pathogens

- Decree of the Russian President on ensuring the fulfillment of international obligations in the area of biological weapons, April 11, 1992 (Decree 390)
- Procedures for controlling export from the Russian Federation of disease agents, their genetically altered forms, and fragments of genetic material that can be used for developing bacteriological (biological) and toxin weapons, November 20, 1992 (Decision of the Russian Government, No. 892)
- Licensing and establishing quotas for exports and imports of biological goods and services, included in instructions of the State Customs Committee, No. 610 of December 12, 1992
- Federal law on state regulation in the area of genetic engineering, June 5, 1996 (adopted by the state Duma)
- Safety of microorganisms of Group I-II pathogenicity, sanitary regulations of 1994, Sanitary Epidemiology Service of Russia
- Interim regulations concerning dangerous work with recombinant DNA, Scientific Center for Biological Research of the Soviet Academy of Sciences, Pushchino, 1978 (prepared by an interagency council)
- Penalties for crimes against the peace and security of mankind: Production or proliferation of weapons of mass destruction, Sections 355 and 356 of the Russian Criminal Code of 1996.

NOTE: These laws, decrees, and regulations have been identified by Russian specialists as being of particular relevance to bilateral cooperation directed to research on dangerous pathogens.

Project Development Activities

During the early years, a variety of activities will be particularly important in developing proposals for joint research and in matching appropriate collaborators. Annual reviews of ongoing projects can help guide selection of future high-priority research themes. Also, the overall approach should be reviewed in depth at the end of the second year and adjusted as necessary.

In addition, the following types of project development activities should be carried out:

- Brief exchange visits to enable researchers from the two countries to develop proposals for submission to funding competitions;
- Travel grants for Russian scientists to participate in scientific conferences in the United States, where they can make contacts and become aware of the state of international science in their fields; and
- Joint scientific workshops to explore new areas for possible projects, including workshops that build on the results of completed projects.

Estimated Cost

The estimated annual cost to the United States of a *Pathogens Initiative* is $6.0 million in the first year (FY 1998), $7.0 million in the second year, and $8.5 million per year in the third, fourth, and fifth years. The steady-state annual costs for the final three years will be as follows:

- Four and a half million dollars (53 percent) to support 15 new projects each year at Russian research institutions throughout the three-year project lifetime. The total funding of $4.5 million will be committed at the beginning but disbursed over the course of the projects. Disbursement, of course, will depend on performance in accordance with agreed-upon work plans.

- Two and a half million dollars (29 percent) to support U.S. collaborators and exchange visits associated with the 15 projects for three years, with the entire amount of funds again committed but not disbursed at the beginning.
- One-half million dollars (6 percent) to support (1) panels of U.S. experts to review project proposals, (2) joint U.S.-Russian workshops to identify priority areas for collaboration, and (3) exploratory visits by U.S. specialists to Russian institutions with largely unknown capabilities, including, if possible, MOD institutes.
- One million dollars (12 percent) for program evaluation, financial management, and related support activities for the *Pathogens Initiative*, involving three full-time staff members.

During the first two years of the *Pathogens Initiative*, project costs will be lower and project development costs will be higher. Thus, the recommended funding level of $6 million for FY 1998 assumes that only 10 projects are initiated; the level of $7 million for FY 1999 assumes 12 projects, leading to 15 new projects in each of the final three years at an annual cost of $8.5 million. (Table E-3 lists the allocation of funds per fiscal year.) The Russian financial contributions will cover primarily (1) the pension, health, and related benefits packages for Russian participants and (2) indirect project costs incurred at Russian facilities because the U.S. overhead contribution will be only about 7 percent of the total project costs. In addition, Russian waivers of value-added taxes and personal income taxes, in a sense, place a financial burden on the Russian government.

Anticipated Results

The foregoing approach will represent a significant commitment by both the United States and Russia to expand research activities and exchange information on biosafety controls over dangerous pathogens. As such, it would advance both the national security and the public health agendas of the two countries. Also, invited efforts would be significant in setting the stage for sustained long-term efforts after the five-year initiative.

The *Pathogens Initiative* is designed to help reduce the likelihood of proliferation of dangerous technologies that are extremely difficult to control, to encourage a concentration of Russian activities at carefully selected facilities with high scientific potential, and to encourage reconfiguration of former Soviet BW facilities to address new public health challenges. It also should contribute to building confidence at the government and laboratory levels about the legitimacy of activities that are under way.

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Phase 2: An Era of Sustained Cooperation

THE UNCERTAIN FUTURE OF RUSSIA

Predicting conditions in Russia 5 to 10 years into the future is uncertain. Russia's national security apparatus, its economic reform agenda, and even its system of political governance are under considerable stress; changes in all of these areas are likely. Depending on the character of such changes, the consequences for defense scientists and public health activities in that country could be substantial. Program recommendations for the distant future concerning national security and public health issues thus should be flexible.

At the same time, U.S.-Russian relations are continually evolving, with bilateral cooperation in areas of national security being particularly sensitive to the state of political relations. In addition, bilateral cooperation directed toward dangerous pathogens cannot be isolated from diplomatic progress in resolving disagreements about compliance with the Biological Weapons Convention (BWC). The committee believes that an ideal outcome involving the BWC and expanded bilateral cooperation would be a synergistic effect, with high-payoff scientific cooperation improving the climate for diplomatic progress and improved political understanding paving the way for broader scientific interaction. The bilateral cooperation envisaged would be a tangible manifestation of U.S. and Russian commitments to Article X of the BWC, which calls for cooperation in the prevention of diseases.

Another area of uncertainty is the future interest of countries in addition to the United States and Russia in a global approach for expanding activities directed toward dangerous pathogens. Whatever the level of interest, however, there is no substitute for U.S. leadership in encouraging Russia to adopt transparency measures, such as those described below, for a broad range of facilities and activities. Thus, efforts to globalize activities should be welcomed, but they are not a substitute for strengthening U.S.-Russian cooperation.

A MODEL FOR SUSTAINED COOPERATION

Despite the foregoing uncertainties, the committee decided to offer a model of a desirable and realistic program of sustained bilateral cooperation. Such a model, referred to here as Phase 2, could provide a goal toward which U.S. and Russian officials and specialists can direct their energies. Ideally, as the *Pathogens Initiative* carried out during Phase 1 approaches its end in fiscal year (FY) 2002, the enthusiasm in both countries for bilateral cooperation should have reached such a high level that Phase 2 activities can build on past successes without interruption.

Development of this model does not mean that the *Pathogens Initiative* would be useful only if a Phase 2 program develops beginning in 2003. Indeed, the benefits of the *Pathogens Initiative* identified in previous chapters should be realized in both Phase 1 and Phase 2. At the same time, a Phase 2 program could enable the two countries, as well as others, to utilize these benefits more fully and make additional contributions to international security, economic development, public health, and international science.

ORGANIZATIONAL ARRANGEMENTS FOR A PHASE 2 PROGRAM

If bilateral cooperation develops rapidly as a result of the *Pathogens Initiative*, the intergovernmental coordinating mechanism suggested in Chapter 3 becomes increasingly important. During Phase 2, a formal structure for intergovernmental coordination would be essential.

One approach for Phase 2 would be to establish an intergovernmental commission, supported by national coordinating bodies, to guide and coordinate cooperative efforts related to dangerous pathogens. The national security and public health aspects of a significantly expanded program of cooperation appear sufficiently important to warrant consideration of a commission dedicated exclusively to this topic. Although the two governments might decide to use another approach, for the purposes of this discussion it is assumed that a commission would be the coordination mechanism of choice.

From the beginning, the commission would be aware of all joint programs involving dangerous pathogens, but it would be committed to facilitating, not complicating, implementation of previously existing bilateral programs. The commission would be responsible for a variety of activities such as the following.

- Establishing priorities and providing overall guidance for all aspects of cooperation—both new and existing activities—and, on a selective basis, reviewing and evaluating progress in implementing activities of special interest
- Approving new cooperative activities
- Making financial commitments for cooperative activities
- Ensuring coordination between new projects and related existing projects and assisting the arrangement of logistics support
- Disseminating both scientific reports and public information about activities of broad interest
- Developing bilateral arrangements that address issues such as intellectual property rights, mechanisms for the rapid importation of essential equipment and supplies, and living accommodations for visiting scientists and their families.

Much of the technical work of the commission would be carried out by bilateral expert groups in areas such as research cooperation, joint efforts in epidemiology, and common requirements for biosafety. Some topics of likely interest to such groups are addressed later in the discussion of technical aspects of the program.

The national coordinating body in the United States should build on experience during the *Pathogens Initiative,* which calls for collaborative efforts of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), and nongovernment sector. Coordination of bilateral and multilateral activities would probably require greater attention during Phase 2. Also, linkages with joint efforts on other public health concerns should be strong.

GENERAL CHARACTERISTICS OF PHASE 2

Given the legacy of mutual mistrust in this field, an era of sustained cooperation should emphasize transparency at several levels. Building on the initial experience in implementing transparency arrangements associated with specific joint projects, Phase 2 would call for broader transparency arrangements for handling dangerous pathogens at the institutional and national levels, as well as at the project level.

A number of components of the Phase 2 program would build on early experience gained within the framework of the *Pathogens Initiative*. Therefore, details of these activities should be modified as

such experience accumulates. Some of the suggested components of Phase 2 may be incorporated at an earlier date into the *Pathogens Initiative* if cooperation develops more rapidly than anticipated.

When fully developed—perhaps in 7 to 10 years—the Phase 2 program would provide a framework for cooperative activities in many aspects of the handling and use of dangerous pathogens in both countries. It would be sufficiently broad in scope that any research, development, or production group with interests in dangerous pathogens in either country would be eligible to participate in cooperative projects. The scientific activities of research teams in both countries would be reported regularly, and the teams would welcome visits to their facilities and detailed discussions of their activities whenever possible. Cooperation would include joint projects at high-hazard facilities and visits by foreign specialists to familiarize themselves with such facilities. It also would include joint efforts to protect and account for any strains of infectious agents that are of mutual interest. Finally, cooperation in biosafety could help ensure that activities involving dangerous pathogens are being handled responsibly in both countries.

The need to protect intellectual property rights and control the dissemination of information that is sensitive because of potential application to biological weapons (BW) is clear. Such requirements, however, should not unnecessarily exclude activities from consideration when cooperative programs are being developed.

By the time Phase 2 is being implemented, the parties to the BWC may have adopted a verification protocol; in this case, procedures concerning access to facilities and information of all types might already have been specified. Such procedures could serve as guidance for implementation of the broadly based program envisaged during Phase 2. If such a protocol is not in place, the commission suggested earlier would be even more important and would have to develop procedures on its own to expand the scope of transparency developed during the *Pathogens Initiative*.

Joint research projects would continue to be the core of activities under the purview of the commission. However, another key aspect in addressing both political and scientific concerns would be steps in both countries to promote effective national regulations for controlling dangerous pathogens. Effective enforcement procedures and sharing of experiences would be particularly important in confidence building.

Over time, the commission would seek to establish additional confidence-building measures. In particular, its goal would be the development of rules to govern a comprehensive exchange of information between the two countries on the handling and use of dangerous pathogens. Ideally, the general characteristics of all significant research and related facilities involved with dangerous pathogens in both countries would be known to each government. The activities of research teams would be regularly reported, as would the strains of infectious agents held for research and related purposes. As with the cooperative activities proposed, measures to ensure adequate protection of intellectual property and other sensitive information in a manner that does not undercut the broader transparency objectives should be developed.[1] Currently, such comprehensive exchange of information is difficult if not impossible to achieve, but as trust between the two countries grows, greater openness should become possible. Moreover, because of concerns about biosafety and terrorism, there is increasing government interest, at least in the United States, in developing such requirements for reporting to national authorities. Thus, there may be both an international and a national basis for bilateral confidence building through expanded exchanges of information.

[1] For example, in the United States a mechanism for protecting proprietary chemicals and providing adequate information for regulatory purposes is well developed and may serve as a precedent for application in the field of biology.

TECHNICAL ASPECTS OF THE PROGRAM

The following sections describe specific approaches in several areas, together with an estimate of their implementation costs to the U.S. government beyond current investments. Adjustment of some of these suggestions and of the cost estimate will inevitably emerge during more detailed program discussions within the U.S. government and with Russian officials.

Research Collaboration

Specialists representing the scientific interests of both countries would meet at least annually to develop agendas for joint research projects for subsequent approval by the two governments. When Phase 2 reaches maturity, the research program would probably be somewhat larger than that of the *Pathogens Initiative*, perhaps 30 percent. Growth to this level is based on several considerations. First, some Russian specialists likely will continue to play key roles in legitimate military research activities during the *Pathogens Initiative* because they are reluctant to abandon their assured sources of income for participation in an international program that may be only temporary. However, after five years of continuous collaboration, these specialists should recognize the importance and sustainability of the program, and some could be expected to become applicants for participation in an expanded program. Second, interest in the United States should grow, particularly if the *Pathogens Initiative* is successful in attracting young U.S. specialists who experience firsthand the benefits of international scientific cooperation. Although the committee supports modest growth, it believes that the program should be capped to ensure the high quality of the projects supported. As noted in Chapter 3, this maximum level of activity is driven by both the importance of limiting the number of facilities involved in work on dangerous pathogens and the manpower pools of specialists available in the two countries to address important public health issues in a highly specialized field.

The following approach, which could be formally established by the commission, appears appropriate for the expanded program during Phase 2:

- Annual or semiannual competitions should be held among Russian institutions and investigators for financial support for projects, including review of applications for support of research on selected pathogens as in the *Pathogens Initiative.* Other dangerous pathogens and cross-cutting research projects that individual investigators propose for support would probably receive much greater emphasis.
- Joint U.S.-Russian peer review panels should be established to select projects for support.
- Final government approvals should be obtained and arrangements made for financial support, including limited U.S. support for Russian activities through the International Science and Technology Center (ISTC) as discussed below or through an equally effective mechanism if the character of the ISTC were to change in the years ahead.

Epidemiology

During Phase 2, special attention would be given to research related to the epidemiology of diseases associated with dangerous pathogens, although some activities might be initiated on a limited scale during Phase 1. Combined capabilities in this field should have major public health benefits in combating the spread of diseases both nationally and worldwide through the following mechanisms.

- Rapid exchanges of significant information on trends and unusual occurrences of diseases associated with dangerous pathogens in the United States and Russia are very important. Some Russian institutions require additional electronic equipment for such communication, and this need should be considered within the context of specific joint projects, as discussed in Chapter 3. Also, joint workshops

would be useful in developing a general consensus on the frequency of and mechanisms for data exchanges and the variety and format of data to be exchanged. This effort should be consistent with the interests of the World Health Organization (WHO), and should support its *Weekly Epidemiology Reports*.

- Related to the international exchange of data is the need to strengthen the internal capabilities of Russia to rapidly assess and process information about disease trends and outbreaks. Projects that enable selected institutes, particularly key members of Biopreparat, to contribute to the national effort of the Ministry of Health should be considered.
- Bilateral workshops and joint research projects should be directed to identifying and developing improved technologies for the diagnosis of agents and diseases of concern.
- During outbreaks in one country of certain diseases linked with dangerous pathogens, specialists in the other country should be encouraged to forward relevant information and identify ways in which they could be most helpful in assessing and responding to such outbreaks. When appropriate, specialists from the other country would be invited to review information and assist in assessments if they have special expertise that could be helpful.
- Russian specialists who are involved in field investigations should be encouraged to apply for participation in CDC training programs.

Research projects related to epidemiology that involve both former Soviet BW institutes and civilian institutions, (for example, institutes of the Biopreparat complex teamed with those of the Ministry of Health or Academy of Medical Sciences) are of special interest. Indeed, strengthening internal organizational linkages within Russia is essential if its defense scientists are to play a significant role in the national public health effort.

Biosafety

The objective of efforts in both countries in the area of biosafety would be to promote consistency in biosafety criteria and practices research laboratories or other facilities that handle dangerous pathogens. Such efforts would help provide assurance (1) that infectious agents are handled in conformance with the WHO *Laboratory Biosafety Manual*[2] and (2) that infectious agents are not transferred to parties who are not authorized to handle them. Also, ensuring that regulations for vaccinations and biosafety procedures are consistent will facilitate reciprocal visits to high-hazard laboratories.

The commission should concentrate on reviewing the development, implementation, and enforcement of national systems in the United States and Russia for controlling the handling and use of dangerous pathogens. It should encourage each government to develop and use approaches that are both effective and transparent, thereby contributing to mutual confidence about compliance with international obligations.

In considering the regulatory framework, the commission might examine, for example, the working lists of infectious agents already set forth in regulations and guidance documents, procedures for registering facilities with national authorities, national requirements for transferring agents nationally and internationally, biosafety criteria for facilities, requirements for disposal of agents, and training of scientists and support personnel.

Among the mechanisms for cooperation related to biosafety are the following approaches:

- Regular exchanges of information on the state of development of national regulatory systems;
- Special exchanges of data on specific activities of particular interest to each country, such as research being carried out at biocontainment or other specialized facilities; and

[2] World Health Organization. 1993. *Laboratory Biosafety Manual,* 2nd Ed. Geneva: WHO.

- Reciprocal visits to selected facilities by biosafety experts on the basis of invitation.

ESTIMATED COSTS

It is expected that as Phase 2 is developed, the Russian participating institutions will be in a position to pay increasingly more of their costs of these cooperative activities. Also, an orderly transition between funding of the *Pathogens Initiative* and financial support for projects in Phase 2 is recommended. In particular, as indicated in Table E-2, the funding of three-year projects during the last two years of the *Pathogens Initiative* should provide an important base of activities for the first two years of Phase 2. The time needed for full development of Phase 2 depends in large measure on the Russian economy and the priority given to efforts directed toward dangerous pathogens.

Because the Russian economy will probably remain weak for a decade or more, U.S. support will be necessary for some Russian activities. In particular, U.S. contributions to Russian expenses might concentrate on (1) purchases of specialized equipment and supplies for experiments in Russia that are directly linked to experiments in the United States and (2) international travel of selected Russian participants who otherwise might not be able to travel to the United States. However, U.S. funds should be used primarily to cover the costs of U.S. participants.

Without considering inflation, the cost to the United States of carrying out activities during Phase 2 is estimated at approximately $10 million per year. About $5 million (50 percent) would support the expenses of U.S. collaborators, with each of an estimated 60 collaborators (20 new collaborators undertaking three-year projects each year) receiving an average of $80,000 per year for their activities. An additional $2 million (20 percent) would be for administrative expenses related to U.S. participation in the commission and its expert groups, which would have five full-time staff members. About $1 million (10 percent) would be used for workshops, project development activities, and planning and evaluation meetings between Russian and U.S. specialists. The remaining $2 million (20 percent) would support the requirements of Russian specialists that are beyond their own means: small pieces of equipment for experiments of special interest to the United States and associated project related international travel for some participants (at an estimated cost of $35,000 per year per project).

Sustained U.S. funding for Phase 2 would undoubtedly require agreement between the executive branch and Congress on a line item in the budget of a selected agency. It is premature to speculate which agency should have financial responsibility.

ANTICIPATED BENEFITS

The Phase 2 program would provide financial, scientific, and information-sharing incentives for the two countries to broaden and sustain linkages between their specialists. The impact of specific joint efforts on public health and other problems is difficult to predict, but Russian and U.S. specialists are in a strong position to contribute substantially in this area of increasing worldwide concern.

A likely effect of a sustained program would be adjustment of the structure of the Russian research enterprise dealing with dangerous pathogens. Research projects would be increasingly concentrated at a handful of the best institutions in the country that emerge as centers of excellence. Some weaker institutions would slowly lose their ability to conduct research on dangerous pathogens and would have even greater difficulty commanding financial support for such work than during the current crisis period.

Special efforts would be necessary to ensure that the stronger institutions are prepared to absorb some scientists from the weaker institutes lest they be tempted to transfer their know-how to states of

proliferation concern. Although consolidation in the Russian research complex would appear to be inevitable, such consolidation should be carefully managed.

If the United States and Russia are able to work together constructively over the long term, the tone of international diplomacy in this field could be significantly improved, resulting in new and important mitigation of the threat of proliferation and terrorism and improved U.S.-Russian relations in an area that too frequently has been punctuated with acrimony. In addition, long-term joint efforts would make major contributions to reducing global risks from emerging and reemerging infectious diseases.

A
Committee and Staff Biographies

COMMITTEE MEMBERS

Joshua Lederberg (NAS, IOM), *chair*, is Professor Emeritus and Raymond and Beverly Sackler Foundation Scholar at the Rockefeller University. In 1958 he received the Nobel Prize in Physiology or Medicine for his work in bacterial genetics. He has been active in many national and international science policy deliberations, especially at the National Institutes of Health (NIH) and World Health Organization (WHO). He served as a consultant to the Arms Control and Disarmament Agency during negotiation of the 1972 Biological and Toxin Weapons Convention (BWC), and he currently serves on the Defense Science Board.

John D. Steinbruner, *vice-chair*, is a Senior Fellow and former Director of the Foreign Policy Studies Program at the Brookings Institution. He has held faculty positions at Yale University, Harvard University, and Massachusetts Institute of Technology. A political scientist, he has written extensively on arms control and security issues, including problems of command and control and crisis decision making. He is a member of the Defense Policy Board.

Barry Bloom (NAS, IOM) is Investigator at the Howard Hughes Medical Institute of the Albert Einstein College of Medicine. He has received numerous awards for his work in immunology and infectious diseases, including the Bristol-Myers Squibb Award. He has been active in the programs of WHO.

Gail Cassell (IOM) is Chair of the Department of Microbiology and Charles H. McCauley Professor of Microbiology at the University of Alabama-Birmingham. She has received a number of awards for her research in infectious diseases and is a recent past President of the American Society for Microbiology. She has been active in national and international policy deliberations, including those of NIH and the U.S.-Japan Cooperative Medical Science Program. She is also a member of the International Science and Technology Center Science Advisory Committee and a member of the steering committee for the U.S.-Japan Cooperative Medical Science Program. She is a recent chair of the Board of Scientific Counselors of the National Center for Infectious Diseases of the Centers for Disease Control and Prevention (CDC).

Robert Chanock (NAS) is Chief of the Laboratory of Infectious Diseases of the National Institute of Allergy and Infectious Diseases of NIH. He has received numerous awards for his work in virology and infectious disease research, including the Bristol-Myers Squibb Award for Distinguished Achievement in Infectious Disease Research, the Robert Koch Medal of the Robert Koch Foundation, the ICN International Prize in Virology, and the Albert Sabin Gold Medal of the Albert Sabin Vaccine Foundation. He has been active in WHO and in national policy discussions.

R. John Collier (NAS) is Professor of Microbiology and Molecular Genetics at Harvard Medical School. His career has been largely devoted to research on the structures and actions of bacterial toxins. He has received a number of awards during his career including the Eli Lilly Award in Microbiology and Immunology and the Paul Ehrlich Prize.

Maurice R. Hilleman (NAS) is Director (formerly Senior Vice President) of the Merck Institute at Merck Research Laboratories in West Point, Pennsylvania. His career has been in basic and applied research on viruses, vaccines, immunology, and cancer. He is a long-time adviser to many health agencies including the Department of Health and Human Services, WHO, Overseas Medical Research Laboratory Committee of the Department of Defense (DOD), and special committees of the NAS and IOM.

Peter B. Jahrling is Scientific Adviser and Senior Research Scientist at the United States Army Medical Research Institute of Infectious Diseases (USAMRIID). He is head of the WHO collaborating center on arbovirus and hemorrhagic fever virus research at USAMRIID and a member of the Committee on Return of Biological Samples of the National Research Council's (NRC's) Space Studies Board. He serves as a guest editor for a number of journals including the third and fourth editions of the *Biosafety in Microbiological and Biomedical Laboratories*. His research interests include development of vaccines, antiviral drugs, and effective treatment strategies for Ebola, Marburg, Lassa, and orthopox viruses.

James Leduc is Associate Director for Global Health in the National Center for Infectious Diseases at CDC. He is a fellow of the American College of Epidemiology and has received numerous awards for outstanding work in epidemiology. He has served as a Medical Officer of WHO and as an Officer at the United States Army Medical Research and Development Command. His research interests include epidemiology of virus diseases, especially viral hemorrhagic fevers and new, emerging and reemerging diseases.

Matthew Meselson (NAS, IOM) is Thomas Dudley Cabot Professor of Natural Sciences at Harvard University and codirector of the Harvard-Sussex program on chemical and biological warfare armament and arms limitation. He has conducted research mainly in the field of molecular genetics and is recipient of the NAS Award in Molecular Biology, the Eli Lilly Award in Microbiology, and the Thomas Hunt Morgan Medal of the Genetics Society of America. He is a member of the Royal Society and the Academie des Sciences and has served as a consultant on chemical and biological weapons matters to U.S. government agencies.

Thomas Monath is Vice President of Research and Development at OraVax and Adjunct Professor at the Harvard School of Public Health. He has been engaged in programs of WHO and the National Vaccines Advisory Committee. He was formerly director of the Division of Vector-Borne Infectious Diseases, CDC, and Chief of Virology, USAMRIID. His research has included work on arboviruses, viral hemorrhagic fevers, bubonic plague, and other zoonotic diseases. He has served on various committees dealing with biological weapons (BW) issues.

Frederick A. Murphy is Professor at the School of Veterinary Medicine at the University of California-Davis. Formerly, he was dean of the school and earlier he was the director of the National Center for Infectious Diseases at CDC. He is recipient of the Presidential Rank Award and is a member of the German Academy of Natural Sciences. He has been a leader in viral pathogenesis, viral characterization, and taxonomy; his interests include public health policy, vaccine development, and new, emerging and reemerging diseases.

Major General Philip K. Russell (retired U.S. Army) is Professor of International Health at the School of Hygiene and Public Health, Johns Hopkins University. He received the Distinguished Service Medal before retiring from military service. He has served on numerous scientific committees including advisory committees to the CDC and WHO. He was also involved in the establishment of medical research facilities at military bases around the world.

Alexis Shelokov is Director of Medical Affairs with the Biologicals Development Center of the Salk Institute. He served as a member of the Expert Working Group on Biological and Toxin Weapons Verification of the Federation of American Scientists. He has been involved in the activities of WHO, NIH, and the U.S.-Japan Cooperative Medical Program. In addition, he served as the chairman of U.S. delegations on hemorrhagic fevers to the Soviet Union in 1965 and 1969.

STAFF MEMBERS

Christopher P. Howson is Director of the Board on International Health of the IOM. In his 11 years at NAS, he has directed 15 projects and in 1993 served as acting director of the IOM Medical Follow-up Agency. Before coming to NAS, he was senior epidemiologist at the American Health Foundation in New York City. He holds a Ph.D. in epidemiology from the University of California at Los Angeles.

Jo L. Husbands is Director of the NAS Committee on International Security and Arms Control. Before assuming that position, she was director of the NRC's Project on Democratization and senior research associate for its Committee on International Conflict and Cooperation. She holds a Ph.D. in political science from the University of Minnesota.

Glenn E. Schweitzer is Director of the Office for Central Europe and Eurasia of the National Research Council. From 1963 to 1966, he served as the first science officer at the American Embassy in Moscow, and from 1992 to 1994 he was the first executive director of the International Science and Technology Center in Moscow. He has also served as director of the Office of Toxic Substances and director of the Environmental Monitoring Systems Laboratory-Las Vegas of the U.S. Environmental Protection Agency.

Chaarles G. Fogelgren is Research Assistant for the NAS Committee on International Security and Arms Control. He holds a B.A. in anthropology from The George Washington University. His interests include chemical and biological weapons disarmament, evolution, ethics, parasitology, and emerging and reemerging diseases.

B
Extract from Statement of Work of DOD/NAS Contract

SCOPE

The CTR program is working with the Russian Federation to expedite the dismantlement of weapons of mass destruction, to encourage nonproliferation, and to promote conversion of military capabilities to peaceful, civilian applications. These efforts will support the CTR program by developing a cooperative support and research program to assist in conversion of the FSU BW personnel and facilities by redirecting work to public health and other peaceful, civilian research programs. The program will be executed by the NAS. NAS, the National Academy of Engineering, IOM, and the National Research Council will collaborate on this project.

OBJECTIVES

The basic objective of this effort is to support the conversion of former Soviet BW research personnel to work on international public health issues. The specific objective is to engage Russian BW researchers in continuing collaborative projects with the West as part of the global effort for research, surveillance, and monitoring of new, emerging and reemerging diseases. Some existing diseases that might be subjects for cooperative work include hantavirus and broader classes of hemorrhagic fevers, tick-borne encephalitis, malaria, tuberculosis, and human immunodeficiency virus (HIV)/AIDS. The specific types of research involved could include work on (1) surveillance and monitoring methods, (2) studies of pathogenesis, (3) diagnostic tests, (4) treatments, and (5) new vaccines.

C
Consultations and Visits

CONSULTATIONS IN UNITED STATES

Discussions with government organizations

- National Security Council
- Department of Defense
    - Office of the Secretary of Defense
    - Cooperative Threat Reduction Program Office
    - Office for International Security Policy
    - Defense Special Weapons Agency
    - Special Operations in Low Intensity Conflict
- United States Army Medical Research Institute of Infectious Diseases
- Department of State
    - Office of the Coordinator for Assistance and Cooperation with the former Soviet Union
    - Bureau of Political and Military Affairs
- Arms Control and Disarmament Agency
- Department of Energy
    - Initiatives for Proliferation Prevention
    - Chemical/Biological Nonproliferation Program
- Department of Commerce
    - Materials Technical Advisory Committee

Other government organizations providing information

- National Institutes of Health
- United States Deparment of Agriculture
- National Science Foundation
- Centers for Disease Control and Prevention
- National Aeronautics and Space Administration

Discussions with nongovernment organizations

- Civilian Research and Development Foundation
- Chemical and Biological Arms Control Institute
- Stimson Center
- University of Maryland

Discussions with other organizations

- United Nations Centre for Disarmament Affairs
- European Commission: DG XII

CONSULTATIONS AND VISITS IN RUSSIA

Special activities

- Roundtable at Petrovo-Dalnyee organized by Biopreparat with officials from Biopreparat and the President's Committee for Conventional Problems of Chemical and Biological Weapons and scientists from a variety of Russian research institutes
- Meeting in Moscow organized by the NAS with representatives from Biopreparat and several institutes of the Biopreparat complex

- International symposium in the Kirov region organized by the International Science and Technology Center (ISTC) with representatives of more than a dozen research institutions

Meetings

- Biopreparat
- Ministry of Health with representatives of several institutes of the ministry
- Russian Academy of Medical Sciences with representatives of several institutes of the academy
- Ministry of Science and Technology
- Russian Academy of Sciences
- Member of Defense Council
- Staff member of Duma Armed Services Committee
- ISTC
- U.S. Embassy: Science Section and Office of Defense Attaché

Visits for scientific discussions

- State Research Center for Applied Microbiology, Obolensk
- "Vector" State Research Center for Virology and Biotechnology, Koltsovo

Familiarization visits

- Volgo-Vyatka Applied Biotechnology Center, Kirov
- Biochemical Plant, Kirov
- Sanitary-Epidemiology Center, Kirov

D

Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous, or Other Gases, and of Bacteriological Methods of Warfare

Signed at Geneva June 17, 1925
Entered into force February 8, 1928
Ratification advised by the U.S. Senate December 16, 1974
Ratified by U.S. President January 22, 1975
U.S. ratification deposited with the government of France April 10, 1975
Proclaimed by U.S. President April 29, 1975

The Undersigned Plenipotentiaries, in the name of their respective Governments:

Whereas the use in war of asphyxiating, poisonous or other gases, and of all analogous liquids, materials or devices, has been justly condemned by the general opinion of the civilized world; and

Whereas the prohibition of such use has been declared in Treaties to which the majority of Powers of the World are Parties; and

To the end that this prohibition shall be universally accepted as a part of International Law, binding alike the conscience and the practice of nations;

Declare:

That the High Contracting Parties, so far as they are not already Parties to Treaties prohibiting such use, accept this prohibition, agree to extend this prohibition to the use of bacteriological methods of warfare and agree to be bound as between themselves according to the terms of this declaration.

The High Contracting Parties will exert every effort to induce other States to accede to the present Protocol. Such accession will be notified to the Government of the French Republic, and by the latter to all signatory and acceding Powers, and will take effect on the date of the notification by the Government of the French Republic.

The present Protocol, of which the French and English texts are both authentic, shall be ratified as soon as possible. It shall bear today's date.

The ratifications of the present Protocol shall be addressed to the Government of the French Republic, which will at once notify the deposit of such ratification to each of the signatory and acceding Powers.

The instruments of ratification of and accession to the present Protocol will remain deposited in the archives of the Government of the French Republic.

The present Protocol will come into force for each signatory Power as from the date of deposit of its ratification, and, from that moment, each Power will be bound as regards other powers which have already deposited their ratifications.

IN WITNESS WHEREOF the Plenipotentiaries have signed the present Protocol.

DONE at Geneva in a single copy, this seventeenth day of June, One Thousand Nine Hundred and Twenty-Five.

Source: U.S. Arms Control and Disarmament Agency

E

Convention on the Prohibtion of the Development, Production, and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction

Signed at Washington, London, and Moscow April 10,1972
Ratification advised by U.S. Senate December 16, 1974
Ratified by U.S. President January 22, 1975
U.S. ratification deposited at Washington, London, and Moscow March 26, 1975
Proclaimed by U.S. President March 26, 1975
Entered into force March 26, 1975

The States Parties to this Convention

Determined to act with a view to achieving effective progress towards general and complete disarmament, including the prohibition and elimination of all types of weapons of mass destruction, and convinced that the prohibition of the development, production and stockpiling of chemical and bacteriological (biological) weapons and their elimination, through effective measures, will facilitate the achievement of general and complete disarmament under strict and effective international control,

Recognizing the important significance of the Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare, signed at Geneva on June 17, 1925, and conscious also of the contribution which the said Protocol has already made, and continues to make, to mitigating the horrors of war,

Reaffirming their adherence to the principles and objectives of that Protocol and calling upon all States to comply strictly with them,

Recalling that the General Assembly of the United Nations has repeatedly condemned all actions contrary to the principles and objectives of the Geneva Protocol of June 17, 1925,

Desiring to contribute to the strengthening of confidence between peoples and the general improvement of the international atmosphere,

Desiring also to contribute to the realization of the purposes and principles of the Charter of the United Nations,

Convinced of the importance and urgency of eliminating from the arsenals of States, through effective measures, such dangerous weapons of mass destruction as those using chemical or bacteriological (biological) agents,

Recognizing that an agreement on the prohibition of bacteriological (biological) and toxin weapons represents a first possible step towards the achievement of agreement on effective measures also for the prohibition of the development, production and stockpiling of chemical weapons, and determined to continue negotiations to that end,

Determined, for the sake of all mankind, to exclude completely the possibility of bacteriological (biological) agents and toxins being used as weapons,

Convinced that such use would be repugnant to the conscience of mankind and that no effort should be spared to minimize this risk,

Have agreed as follows:

Article I

Each State Party to this Convention undertakes never in any circumstances to develop, produce, stockpile or otherwise acquire or retain:

(1) Microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes;

(2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.

Article II

Each State Party to this Convention undertakes to destroy, or to divert to peaceful purposes, as soon as possible but not later than nine months after the entry into force of the Convention, all agents, toxins, weapons, equipment and means of delivery specified in article I of the Convention, which are in its possession or under its jurisdiction or control. In implementing the provisions of this article all necessary safety precautions shall be observed to protect populations and the environment.

Article III

Each State Party to this Convention undertakes not to transfer to any recipient whatsoever, directly or indirectly, and not in any way to assist, encourage, or induce any State, group of States or international organizations to manufacture or otherwise acquire any of the agents, toxins, weapons, equipment or means of delivery specified in article I of the Convention.

Article IV

Each State Party to this Convention shall, in accordance with its constitutional processes, take any necessary measures to prohibit and prevent the development, production, stockpiling, acquisition, or retention of the agents, toxins, weapons, equipment and means of delivery specified in article I of the Convention, within the territory of such State, under its jurisdiction or under its control anywhere.

Article V

The States Parties to this Convention undertake to consult one another and to cooperate in solving any problems which may arise in relation to the objective of, or in the application of the provisions of, the Convention. Consultation and cooperation pursuant to this article may also be

undertaken through appropriate international procedures within the framework of the United Nations and in accordance with its Charter.

Article VI

(1) Any State Party to this Convention which finds that any other State Party is acting in breach of obligations deriving from the provisions of the Convention may lodge a complaint with the Security Council of the United Nations. Such a complaint should include all possible evidence confirming its validity, as well as a request for its consideration by the Security Council.

(2) Each State Party to this Convention undertakes to cooperate in carrying out any investigation which the Security Council may initiate, in accordance with the provisions of the Charter of the United Nations, on the basis of the complaint received by the Council. The Security Council shall inform the States Parties to the Convention of the results of the investigation.

Article VII

Each State Party to this Convention undertakes to provide or support assistance, in accordance with the United Nations Charter, to any Party to the Convention which so requests, if the Security Council decides that such Party has been exposed to danger as a result of violation of the Convention.

Article VIII

Nothing in this Convention shall be interpreted as in any way limiting or detracting from the obligations assumed by any State under the Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare, signed at Geneva on June 17, 1925.

Article IX

Each State Party to this Convention affirms the recognized objective of effective prohibition of chemical weapons and, to this end, undertakes to continue negotiations in good faith with a view to reaching early agreement on effective measures for the prohibition of their development, production and stockpiling and for their destruction, and on appropriate measures concerning equipment and means of delivery specifically designed for the production or use of chemical agents for weapons purposes.

Article X

(1) The States Parties to this Convention undertake to facilitate, and have the right to participate in, the fullest possible exchange of equipment, materials and scientific and technological information for the use of bacteriological (biological) agents and toxins for peaceful purposes. Parties to the Convention in a position to do so shall also cooperate in contributing individually or together with other States or international organizations to the further development and application of scientific discoveries in the field of bacteriology (biology) for prevention of disease, or for other peaceful purposes.

(2) This Convention shall be implemented in a manner designed to avoid hampering the economic or technological development of States Parties to the Convention or international

cooperation in the field of peaceful bacteriological (biological) activities, including the international exchange of bacteriological (biological) agents and toxins and equipment for the processing, use or production of bacteriological (biological) agents and toxins for peaceful purposes in accordance with the provisions of the Convention.

Article XI

Any State Party may propose amendments to this Convention. Amendments shall enter into force for each State Party accepting the amendments upon their acceptance by a majority of the States Parties to the Convention and thereafter for each remaining State Party on the date of acceptance by it.

Article XII

Five years after the entry into force of this Convention, or earlier if it is requested by a majority of Parties to the Convention by submitting a proposal to this effect to the Depositary Governments, a conference of States Parties to the Convention shall be held at Geneva, Switzerland, to review the operation of the Convention, with a view to assuring that the purposes of the preamble and the provisions of the Convention, including the provisions concerning negotiations on chemical weapons, are being realized. Such review shall take into account any new scientific and technological developments relevant to the Convention.

Article XIII

(1) This Convention shall be of unlimited duration.

(2) Each State Party to this Convention shall in exercising its national sovereignty have the right to withdraw from the Convention if it decides that extraordinary events, related to the subject matter of the Convention, have jeopardized the supreme interests of its country. It shall give notice of such withdrawal to all other States Parties to the Convention and to the United Nations Security Council three months in advance. Such notice shall include a statement of the extraordinary events it regards as having jeopardized its supreme interests.

Article XIV

(1) This Convention shall be open to all States for signature. Any State which does not sign the Convention before its entry into force in accordance with paragraph (3) of this Article may accede to it at any time.

(2) This Convention shall be subject to ratification by signatory States. Instruments of ratification and instruments of accession shall be deposited with the Governments of the United States of America, the United Kingdom of Great Britain and Northern Ireland and the Union of Soviet Socialist Republics, which are hereby designated the Depositary Governments.

(3) This Convention shall enter into force after the deposit of instruments of ratification by twenty-two Governments, including the Governments designated as Depositary of the Convention.

(4) For States whose instruments of ratification or accession are deposited subsequent to the entry into force of this Convention, it shall enter into force on the date of the deposit of their instruments of ratification or accession.

(5) The Depositary Governments shall promptly inform all signatory and acceding States of the date of each signature, the date of deposit of each instrument of ratification or of accession and the date of the entry into force of this Convention, and of the receipt of other notices.

(6) This Convention shall be registered by the Depositary Governments pursuant to Article 102 of the Charter of the United Nations.

Article XV

This Convention, the English, Russian, French, Spanish and Chinese texts of which are equally authentic, shall be deposited in the archives of the Depositary Governments. Duly certified copies of the Convention shall be transmitted by the Depositary Governments to the Governments of the signatory and acceding states.

IN WITNESS WHEREOF the undersigned, duly authorized, have signed this Convention.

DONE in triplicate, at the cities of Washington, London and Moscow, this tenth day of April, one thousand nine hundred and seventy-two.

Source: U.S. Arms Control and Disarmament Agency

F

Australia Group

Chaired by Australia, the "Australia Group" (AG) is an informal forum of states whose goal is to discourage and impede chemical weapons (CW) proliferation by harmonizing national export controls on CW precursor chemicals, sharing information on target countries, and seeking other ways to curb the use of CW.

The Group was formed in 1984 as a result of CW use in the Iran-Iraq war. Members meet annually in Paris, where the 1925 Geneva Protocol is deposited. The Group's actions are viewed as complementary measures in support of the 1925 Geneva Protocol, the 1972 Biological and Toxins Weapons Convention and the 1993 Chemical Weapons Convention.

There are presently 30 members of the Group, including: EC-12, Australia, Argentina, Austria, Czech Republic, Hungary, Iceland, New Zealand, Japan, Canada, Norway, Finland, Sweden, Switzerland, Poland, Romania, the Slovak Republic, South Korea, and the United States. Requests by other states to join the Group are considered on a case-by-case basis.

The Group has no charter or constitution. It operates by consensus. On December 10, 1992, the AG issued its first joint background paper on the Group's activities.

The Group has established common export controls for chemical and biological weapons nonproliferation purposes. For CW, members of the AG control a list of 54 chemical precursors and a list of CW-related production equipment as well. For BW, members have established export controls on certain microorganisms, toxins, and equipment that could be used in a BW program.

In tandem with export controls, the AG has periodically used warning mechanisms to sensitize its public to CBW proliferation. The Group has issued an informal "warning list" of dual-use CW precursors and bulk chemicals, and on CW-related equipment. Members develop and share the warning lists with their chemical industries and ask industry to report on any suspicious transactions. The AG has also used an approach to warn industry, the scientific community, and other relevant groups of the risk of inadvertently aiding BW proliferation.

The Group's meetings focus on sharing information about national export controls, considering proposals for "harmonization"—the adoption of common controls by all members on chemical precursors, equipment, biological weapons related materials, and considering other measures to address CBW proliferation and use.

LIST OF DUAL-USE BIOLOGICAL EQUIPMENT FOR EXPORT CONTROL

1. Complete containment facilities at P3, P4 containment level

   Complete containment facilities that meet the criteria for P3 or P4 (BL3, BL4, L3, L4) containment as specified in the WHO Laboratory Biosafety manual (Geneva, 1983) are subject to export control.

2. Fermenters*

Fermenters capable of cultivation of pathogenic micro-organisms, or viruses or of toxin production, without the propagation of aerosols, and having all the following characteristics:

(a) Capacity equal to or greater than 100 litres.

*Sub-groups of fermenters include bioreactors, chemostats and continuous-flow systems.

3. Centrifugal Separators*

Centrifugal separators capable of the continuous separation of pathogenic microorganisms, without the propagation of aerosols, and having all the following characteristics:

(a) Flow rate greater than 100 litres per hour;
(b) Components of polished stainless steel or titanium;
(c) Double or multiple sealing joints within the steam containment area; and
(d) Capable of in-situ steam sterilization in a closed state.

*Centrifugal separators include decanters.

4. Cross-flow filtration equipment

Cross-flow filtration equipment capable of continuous separation of pathogenic microorganisms, viruses, toxins, and cell cultures without the propagation of aerosols, having all the following characteristics:

(a) Equal to or greater than 5 square metres;
(b) Capable of in situ sterilization.

5. Freeze-drying equipment

Steam sterilizable freeze-drying equipment with a condensor capacity greater than 50 kg of ice in 24 hours and less than 1000 kg of ice in 24 hours.

6. Equipment that incorporates or is contained in P3 or P4 (BL3, BL4, L3, L4) containment housing, as follows:

(a) Independently ventilated protective full or half suits; and
(b) Class III biological safety cabinets or isolators with similar performance standards.

7. Aerosol inhalation chambers

Chambers designed for aerosol challenge testing with microorganisms, viruses, or toxins and having a capacity of 1 cubic metre or greater.

The experts propose that the following items be included in awareness-raising guidelines to industry:

1. Equipment for the microencapsulation of live microorganisms and toxins in the range of 1-10 μm particle size, specifically:

(a) Interfacial polycondensors; and
(b) Phase separators.

2. Fermenters of less than 100 litre capacity with special emphasis on aggregate orders or designs for use in combined systems.

3. Conventional or turbulent air-flow clean-air rooms and self-contained fan-HEPA filter units that may be used for P3 or P4 (BL3, BL4, L3, L4) containment facilities.

LIST OF BIOLOGICAL AGENTS FOR EXPORT CONTROL CORE LIST [1]

Viruses

V1. Chikungunya virus
V2. Congo-Crimean haemorrhagic fever virus
V3. Dengue fever virus
V4. Eastern equine encephalitis virus
V5. Ebola virus
V6. Hantaan virus
V7. Junin virus
V8. Lassa fever virus
V9. Lymphocytic choriomeningitis virus
V10. Machupo virus
V11. Marburg virus
V12. Monkeypox virus
V13. Rift Valley fever virus
V14. Tick-borne encephalitis virus (Russian spring-summer encephalitis virus)
V15. Variola virus
V16. Venezuelan equine encephalitis virus
V17. Western equine encephalitis virus
V18. White pox
V19. Yellow fever virus
V20. Japanese encephalitis virus

Rickettsiae

R1. *Coxiella burnetii*
R2. *Bartonella quintana (Rochalimea quintana, Rickettsia quintana)*
R3. *Rickettsia prowasecki*
R4. *Rickettsia rickettsii*

Bacteria

B1. *Bacillus anthracis*
B2. *Brucella abortus*

B3. *Brucella melitensis*
B4. *Brucella suis*
B5. *Chlamydia psittaci*
B6. *Clostridium botulinum*
B7. *Francisella tularensis*
B8. *Burkholderia mallei (Pseudomonas mallei)*
B9. *Burkholderia pseudomallei (Pseudomonas pseudomallei)*
B10. *Salmonella typhi*
B11. *Shigella dysenteriae*
B12. *Vibrio cholerae*
B13. *Yersinia pestis*

Genetically modified microorganisms

G1. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences associated with pathogenicity and are derived from organisms in the core list.

G2. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins in the core list or their subunits.

Toxins as follows and subunits thereof:[2]

T1. Botulinum toxins
T2. *Clostridium perfringens* toxins
T3. Conotoxin
T4. Ricin
T5. Saxitoxin
T6. Shiga toxin
T7. *Staphylococcus aureus* toxins
T8. Tetrodotoxin
T9. Verotoxin
T10. Microcystin (Cyanginosin)
T11. Aflatoxins

---

1. Except where the agent is in the form of a vaccine.
2. Excluding immunotoxins.

WARNING LIST[1]

Viruses

WV1. Kyasanur Forest virus
WV2. Louping ill virus
WV3. Murray Valley encephalitis virus
WV4. Omsk haemorrhagic fever virus
WV5. Oropouche virus
WV6. Powassan virus
WV7. Rocio virus

WV8. St. Louis encephalitis virus

Bacteria

WB1. *Clostridium perfringens**
WB2. *Clostridium tetani**
WB3. Enterohaemorrhagic *Escherichia coli*, serotype 0157, and other verotoxin-producing serotypes
WB4. *Legionella pneumophila*
WB5. *Yersinia pseudotuberculosis*

Genetically modified microorganisms

WG1. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences associated with pathogenicity and are derived from organisms in the warning list.

WG2. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins in the warning list or their subunits.

Toxins as follows and subunits thereof:[2]

WT1. Abrin
WT2. Cholera toxin
WT3. Tetanus toxin
WT4. Trichothecene mycotoxins
WT5. Modeccin
WT6. Volkensin
WT7. Viscum album lectin 1 (Viscumin)

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*The Australia Group recognizes that these organisms are ubiquitous, but, as they have been acquired in the past as part of biological weapons programs, they are worthy of special caution.

1. Except where the agent is in the form of a vaccine.

2. Excluding immunotoxins.

LIST OF ANIMAL PATHOGENS FOR EXPORT CONTROL[1]

Viruses

AV1. African swine fever virus
AV2. Avian influenza virus[2]
AV3. Bluetongue virus
AV4. Foot and mouth disease virus
AV5. Goatpox virus
AV6. Herpesvirus (Aujeszky's disease)
AV7. Hog cholera virus (synonym: swine fever virus)
AV8. Lyssa virus
AV9. Newcastle disease virus

AV10. Peste des petits ruminants virus
AV11. Porcine enterovirus type 9 (synonym: swine vesicular disease virus)
AV12. Rinderpest virus
AV13. Sheeppox virus
AV14. Teschen disease virus
AV15. Vesicular stomatitis virus

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1. Except where the agent is in the form of a vaccine.

2. This includes only those avian influenza viruses of high pathogenicity as defined in EC Directive 92/401EC: "Type A viruses with an IVPI (intravenous pathogenicity index) in 6 week old chickens of greater than 1.2, or Type A viruses HS or H7 subtype for which nucleotide sequencing has demonstrated multiple basic amino acids at the cleavage site of haemagglutinin."

Bacteria

AB3. *Mycoplasma mycoides*

Genetically-modified microorganisms

AG1. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences associated with pathogenicity and are derived from organisms in the list.

CONTROL LIST OF PLANT PATHOGENS FOR EXPORT CONTROL

CORE LIST

Bacteria

PB1. *Xanthomonas albilineans*
PB2. *Xanthomonas campestris* pv. citri

Fungi

PF1. *Colletotrichum coffeanum var. virulans (Colletotrichum kanawae)*
PF2. *Cochliobolus miyabeanus (Helminthosporium oryzae)*
PF3. *Microcyclus ulei (*synonym *Dothidella ulei)*
PF4. *Puccinia graminis (*synonym *Puccinia graminis* f. sp. *tritici)*
PF5. *Puccinia striiformis (*synonym *Pucciniaglumarum)*
PF6. *Pyricularia grisea/Pyricularia oryzae*

Genetically modified Microorganisms

PG1. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences associated with pathogenicity derived from the plant pathogens identified on the export control list.

ITEMS FOR INCLUSION IN AWARENESS-RAISING GUIDELINES

Bacteria

PWB1. *Xanthomonas campestris* pv. oryzae
PWB2. *Xylella fastidiosa*

Fungi

PWF1. *Deuterophoma tracheiphila* (synonym *Phoma tracheiphila*)
PWF2. *Monilia rorei* (synonym *Moniliophthora rorei*)

Viruses

PWV1. Banana bunchy top virus

Genetically modified microorganisms

PWG1. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences associated with pathogenicity derived from the plant pathogens identified on the awareness-raising list.

Source: U.S. Arms Control and Disarmament Agency

G

Conclusions of Roundtable on Bilateral Cooperation to Address the Public Health Aspects of Dangerous Pathogens
(Petrovo-Dalnyee, April 28-29,1997)

1. The Russian participants expressed their appreciation to the National Academy of Sciences and its Institute of Medicine for proposing the Roundtable on a topic of great importance to Russia and the United States. The American participants expressed their appreciation to RAO Biopreparat for organizing the Roundtable and for ensuring excellent working conditions and living arrangements.
2. The presentations and discussions underscored the importance of the contributions of American and Russian scientists to improving prophylaxis, epidemiological monitoring, and therapy of infectious diseases.
3. Expanded bilateral cooperation between American and Russian specialists could combine important and unique national capabilities of the two countries and of the broader international community to improve understanding of the characteristics of dangerous pathogens and to reduce risks to public health and national security.
4. An important confidence-building step would be an expansion of bilateral cooperation at the laboratory level in an atmosphere of transparency, with exchanges of scientists having experience with dangerous pathogens, including specialists who are working on defense topics, as well as other specialists.
5. The participants welcomed the progress in developing the initial collaborative research projects to be supported by the National Academy of Sciences through the International Science and Technology Center and to be carried out by the State Research Center for Virology and Biotechnology "Vector" and the State Research Center for Applied Microbiology.
6. In looking to the future, the participants discussed different approaches to expand cooperation. There are important issues that must be resolved at the governmental level and scientists can assist in identifying such issues as collaboration expands.
7. The Russian participants will establish a small working group to continue to provide suggestions to the National Academy of Sciences during the next several months as to future collaborative activities which would be important in improving the prophylaxis, epidemiological monitoring, and therapy of diseases caused by dangerous pathogens. The National Academy of Sciences will communicate with RAO Biopreparat concerning the next steps in this regard.

Yuri Kalinin
Head of Russian Delegation

John Steinbruner
Head of American Delegation

Petrovo-Dalnyee
April 29, 1997

H

Report of the International Symposium on "Severe Infectious Diseases: Epidemiology, Express-Diagnostics, and Prevention" Nizhne-Ivkino, Kirov Oblast June 16-20, 1997

The participants from a number of countries emphasized the importance of the topics discussed during the symposium, which are set forth in the attached agenda.

The problem of emerging and reemerging infections should be considered a top priority at both the national and international levels. The consequences of unpredictable epidemics which could be caused by these infections are very serious.

The urgent nature of the problem is based on the evolving nature of the genome and biological (e.g., antigenic) characteristics of pathogens. Such changes are the result of dramatic alterations in social and environmental conditions at both local and global levels. The natural migration of animals, the increasing movement of people, and modifications in ecosystems due to anthropogenic activities also contribute to the global spread of numerous zoonoses and zooanthroponoses. It is necessary to anticipate and predict such situations and conduct monitoring at the national and international levels in order to prevent and reduce the scope of epidemic events.

In the case of emergency epidemic situations, it is necessary to ensure adequate and timely diagnostics, as well as reliable vaccines and antimicrobials, including antivirals, and other preparations for saving human and animal lives. In this regard, the following approaches should be directed to the diseases of greatest concern (see Table 1 for examples of diseases):

a) Identify organisms for which vaccines, antiviral preparations, and antibiotics should be developed and specify groups which require immunization.

b) Employ the tremendous power of modern molecular microbiology and immunology toward the conception and design of the most effective, innovative vaccines against the most dangerous pathogens.

c) Apply the new knowledge obtained from basic molecular microbiologic research toward rapid vaccine production technology and effective distribution for the global prevention and control of catastrophic disease episodes.

d) Develop highly sensitive and specific methods of rapid diagnostics.

These areas were discussed in the reports during the symposium.

The reported experiments and data reflected the substantial progress which has been achieved in diagnosing and preventing emerging and reemerging infections. At the same time, a wide range of problems was identified. In some cases, solutions to these problems were proposed.

In addition to reports on fundamental research highlighting the basic pathogenesis of highly dangerous infections, molecular and genetic characteristics of their causative agents, and mechanisms of immunogenesis, attention also focused on results obtained from applied research. Such studies are aimed at improving techniques and methods of rapid diagnostics of highly dangerous infections and indication and identification of relevant pathogens, as well as developing new research efforts in the design of immunological and biological preparations.

The participants recognized the special contributions to public health which defense scientists can make and urged them to direct their efforts to improved prophylaxis, detection, and treatment of highly dangerous pathogens.

The participants of the symposium enthusiastically supported the idea of exchanges of specialists from different countries. It would facilitate the sharing of research results and the search for areas of mutually beneficial scientific cooperation and would provide a basis for joint research.

Expanded educational programs are needed to improve understanding among both health practitioners and the general public about practical measures that can be taken to reduce the risks of infections from dangerous pathogens.

Modern information and communications technologies are providing unprecedented opportunities for direct communications among scientists throughout the world. Governments and private organizations should ensure that these technologies are made available to scientists working on dangerous pathogens.

A continuing high level of attention should be given to all aspects of safe handling of dangerous pathogens, including the safe disposal of contaminated wastes.

Thus, it is clear that scientists must support the battle against epidemics which result in tremendous disasters inflicted on the world's population and cause 16 million deaths every year.

The participants expressed their sincere gratitude to the U.S. National Academy of Sciences and the International Science and Technology Center, which cosponsored the symposium, to the Volga-Vyatka State Scientific Center of Applied Biotechnology, which organized the event, and to the governor of Kirov Region, Academician V.N. Sergeenkov, for his special interest in the symposium.

The participants had an opportunity to visit the Kirov Biochemical Plant, the Vyatka Chamber of Commerce and Industry, and the facilities of the Sanitary Epidemiological Service and the Committee on Ecology in Kirov. Also, the participants welcomed the proposal of the Volgo-Vyatka State Scientific Center for Applied Biotechnology to serve as a point of contact for future cooperation with the region in fields related to the topics discussed at the symposium.

June 20, 1997

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NOTE: This list does not include unregistered exhibitors at the conference.

I
Descriptions of Pilot Projects

Project 1: The study of prevalence, genotype distribution, and molecular variability of isolates of hepatitis C virus in the Asian part of Russia

Description: This project focuses on sequencing and identifying genotypic variants of hepatitis C virus (HCV) in the Asian Russian population to determine the extent of variability of the virus in the region.

Importance: HCV is a serious public health problem in Russia, the United States, and globally. Approximately 2 percent of blood donors in Russia are infected with HCV, resulting in a 20 to 40 percent prevalence of infection in recipients of multiple transfusions. Fifteen isolates of HCV have been partially sequenced to date. This has led to the discovery of several nontypical genotypes that appear to have evolved independently in the isolated populations of Siberia and the Far East. There is a need for additional data on the extent of variability of the virus in Asian Russia (and elsewhere) for three reasons: (1) to determine whether commercially available tests can detect all current genotypic variants of HCV, (2) to ascertain how well vaccines in development will protect against these variants, and (3) and to provide an additional means for estimating the prevalence of HCV infection in the general population. The findings of this project should usefully inform national HCV prevention and control programs.

Project 2: Monkeypox virus genome

Description: This project focuses on sequencing the monkeypox virus genome.

Importance: Monkeypox is a classic emerging infectious disease. Sequencing the monkeypox virus genome will facilitate development of species-specific diagnostics based on polymerase chain reaction. In addition, comparison of the monkeypox virus genome with that of variola (smallpox) may reveal substantial duplication of gene functions, thereby contributing essential information relevant to the planned worldwide destruction of variola in 1999. Better understanding of the relation of structure to function in the monkeypox virus genome is also expected to provide insight into the rational design of effective antiviral drugs and therapeutic strategies for monkeypox and other orthopox viruses.

Project 3: Study of the genetic and serologic diversity of Hantavirus in the Asian part of Russia

Description: This project is cataloguing the genetic and serologic variability of hantaviruses collected from the Asian part of Russia.

Importance: Hemorrhagic fever with renal syndrome is a significant cause of human morbidity and mortality in the Asian part of Russia, with the disease extending to South Korea and China. Strains of classic Hantaan virus, found in China and Korea, are known to occur in far eastern Russia, whereas Puumala virus, predominant in European Russia, extends into Siberia and the Far East. In addition, other newly recognized Hantaviruses such as Khabarovsk virus exist in eastern Russia, but their potential to cause human illness has yet to be determined. Hantaviruses are emerging throughout the world, and it is currently unknown where new Asian strains fit in the phylogenetic tree. This study should yield important information about the serologic and genetic variability of Hantaviruses and help identify rodent hosts and risk factors for this important group of viral pathogens. These findings, in turn, could help inform research and development in support of effective vaccines against Hantavirus infection in the United States and Russia.

Project 4: Development of advanced diagnostic kit for opisthorchiasis in human patients

Description: This project is developing an advanced diagnostic kit for human opisthorchiasis.

Importance: The parasitic liver fluke *Opisthorchis felineus* represents a significant human health problem in much of Russia, with an estimated 10 to 20 million human infections in Siberia alone. Liver flukes in the same family are also found in contaminated fish in the northwestern

United States. Current diagnostic procedures rely on direct stool examination, which is time-consuming, technically difficult, and expensive. An enzyme immunoassay has been developed for serologic diagnosis but is limited in value because it is not able to differentiate between current infections and cured individuals. An effective treatment with phenolics is available, but these drugs are too toxic to use except to treat active infection; thus, there is an urgent need for an improved diagnostic test to differentiate active cases rapidly, accurately, and with minimum cost. Sufficient human samples are readily available to ensure that substantive evaluation of candidate assays will be conducted promptly, with preliminary results likely to be available during 1997.

Project 5: Molecular biological and immunochemical analysis of clinical strains of tuberculosis and mycobacteriosis

Description: This project focuses on characterization of different strains of mycobacteria in Russian patients diagnosed with tuberculosis (TB).

Importance: TB, particularly drug-resistant TB, represents a serious threat to the United States and is increasing in Russia in epidemic proportions. This project is characterizing different strains of mycobacteria isolated from Russian patients diagnosed with TB and is determining the spectrum of drug resistance among them. The relation between strain virulence and the spectrum and degree of drug resistance will be explored by identifying the genes responsible for drug resistance. New antibiotics under development in Russia will be tested for their potency against these clinical strains. This project will help strengthen Russian capability in addressing the emerging TB epidemic in Russia.

Project 6: Investigation of the immunological effectivity of delivery in vivo of the *Brucella* main outer membrane protein by anthrax toxin components

Description: This project is an initial step toward the eventual goal of producing an effective recombinant protein vaccine or vaccine mixture for veterinary use against *Brucella abortus* and for protection of occupationally exposed personnel.

Importance: Human brucellosis is a disease caused by species of the bacterium *Brucella*. In humans it is seriously debilitating but seldom lethal. Its principal reservoirs are cattle, sheep, and swine. Human exposure is principally from direct contact with infected animals and animal products, including consumption of unpasteurized milk and milk products from infected animals. Control of the disease in humans occurs mainly by avoiding the consumption of unpasteurized milk or milk products and contact with infected animals, sacrificing infected animals and herds, and, in areas where brucellosis is endemic, veterinary vaccination. None of the current vaccines against brucellosis is completely satisfactory; their shortcomings include incomplete protection, induction of abortion, and occasional infectivity to humans. This protocol calls for the construction of chimeric genes expressing anthrax lethal factor (LF)-*Brucella* outer membrane protein (OMP) fusion proteins and testing of the resulting chimeric proteins when administered together with anthrax protective factor for immunological effectiveness against *Brucella abortus*. The LF-protective antigen (PA) cell delivery system holds great promise for an improved brucellosis vaccine, in particular, and for more effective disease prevention in the United States and Russia generally.